25-024

ILLINOIS HEALTH FACILITIES AND SERVICES REVIEW BOARD APPLICATION FOR PERMIT

SECTION I. IDENTIFICATION, GENERAL INFORMATION, AND CERTIFICATION
This Section must be completed for all projects.

Facility/Project Identification

Facility Name: UroPartners Imaging Center		
Street Address: 2225 Enterprise Drive, Suite 3510		
City and Zip Code: Westchester, 60154		
County: Cook	Health Service Area: 7	Health Planning Area: 031

Applicant(s) [Provide for each applicant (refer to Part 1130.220)]

Exact Legal Name: UroPartners, LLC
Street Address: 2245 Enterprise Drive, Suite 4506
City and Zip Code: Westchester, 60154
Name of Registered Agent: Neal T. Goldstein
Registered Agent Street Address: 200 S. Wacker Drive, Suite 2700
Registered Agent City and Zip Code: Chicago, 60606
Name of Chief Executive Officer: Richard G. Harris
CEO Street Address: 2245 Enterprise Drive, Suite 4506
CEO City and Zip Code: Westchester, 60154
CEO Telephone Number: (708) 492-0502

Type of Ownership of Applicants

- ☐ Non-profit Corporation
- ☐ For-profit Corporation
- ☒ Limited Liability Company
- ☐ Partnership
- ☐ Governmental
- ☐ Sole Proprietorship
- ☐ Other

- Corporations and limited liability companies must provide an **Illinois certificate of good standing.**
- Partnerships must provide the name of the state in which they are organized and the name and address of each partner specifying whether each is a general or limited partner.

APPEND DOCUMENTATION AS ATTACHMENT 1, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

Primary Contact [Person to receive ALL correspondence or inquiries]

Name: Mark Silberman and Juan Morado Jr.
Title: Partners and CON Counsel
Company Name: Benesch, Friedlander, Coplan and Aronoff
Address: 71 S. Wacker Drive, Suite 1600 Chicago, IL 60606
Telephone Number: (312) 212-4952 and (312) 212-4967
E-mail Address: MSilberman@beneschlaw.com and JMorado@beneschlaw.com
Fax Number: (877) 357-4913

Additional Contact [Person who is also authorized to discuss the application for permit]

Name: Nick Radonjic
Title: General Counsel/Chief Operating Officer
Company Name: UroPartners, LLC
Address: 2245 Enterprise Drive, Suite 4506, Westchester, IL 60154
Telephone Number: (708) 492-0565
E-mail Address: NRadonjic@UroPartners.com
Fax Number: (708) 495-0565

ILLINOIS HEALTH FACILITIES AND SERVICES REVIEW BOARD
APPLICATION FOR PERMIT

SECTION I. IDENTIFICATION, GENERAL INFORMATION, AND CERTIFICATION
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Facility/Project Identification

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Street Address: 2225 Enterprise Drive, Suite 3510
City and Zip Code: Westchester, 60154
County: Cook Health Service Area: 7 Health Planning Area: 031

Applicant(s) [Provide for each applicant (refer to Part 1130.220)]

Exact Legal Name: Solaris Health Holdings, LLC
Street Address: 500 East Broward Boulevard, Suite 2150
City and Zip Code: Fort Lauderdale, 33394
Name of Registered Agent: Illinois Corporation Service Company
Registered Agent Street Address: 801 Adlai Stevenson Drive
Registered Agent City and Zip Code: Springfield, 62703
Name of Chief Executive Officer: Gary Kirsh, MD
CEO Street Address: 500 East Broward Boulevard, Suite 2150
CEO City and Zip Code: Fort Lauderdale, 33394
CEO Telephone Number: (954) 678-4377

Type of Ownership of Applicants

- ☐ Non-profit Corporation
- ☐ For-profit Corporation
- ☒ Limited Liability Company
- ☐ Partnership
- ☐ Governmental
- ☐ Sole Proprietorship
- ☐ Other

- Corporations and limited liability companies must provide an **Illinois certificate of good standing.**
- Partnerships must provide the name of the state in which they are organized and the name and address of each partner specifying whether each is a general or limited partner.

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E-mail Address: NRadonjic@UroPartners.com
Fax Number: (708) 495-0565

Post Permit Contact [Person to receive all correspondence after permit issuance-**THIS PERSON MUST BE EMPLOYED BY THE LICENSED HEALTH CARE FACILITY AS DEFINED AT 20 ILCS 3960]**

Name: Nick Radonjic
Title: General Counsel/Chief Operating Officer
Company Name: UroPartners, LLC
Address: 2245 Enterprise Drive, Suite 4506, Westchester, IL 60154
Telephone Number: (708) 492-0565
E-mail Address: NRadonjic@UroPartners.com
Fax Number: (708) 495-0565

Site Ownership [Provide this information for each applicable site]

Exact Legal Name of Site Owner: Enterprise Centre, LLC
Address of Site Owner: 55 East Jackson Boulevard Chicago, IL 60604
Street Address or Legal Description of the Site: **Proof of ownership or control of the site is to be provided as Attachment 2. Examples of proof of ownership are property tax statements, tax assessor's documentation, deed, notarized statement of the corporation attesting to ownership, an option to lease, a letter of intent to lease, or a lease.**
APPEND DOCUMENTATION AS ATTACHMENT 2, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

Operating Identity/Licensee [Provide this information for each applicable facility and insert after this page.]

Exact Legal Name: UroPartners, LLC

Address: 2245 Enterprise Drive, Suite 4506, Westchester, IL 60154

☐	Non-profit Corporation	☐	Partnership
☐	For-profit Corporation	☐	Governmental
☒	Limited Liability Company	☐	Sole Proprietorship
	Other		☐

- Corporations and limited liability companies must provide an Illinois Certificate of Good Standing.
- Partnerships must provide the name of the state in which organized and the name and address of each partner specifying whether each is a general or limited partner.
- **Persons with 5 percent or greater interest in the licensee must be identified with the % of ownership.**

APPEND DOCUMENTATION AS ATTACHMENT 3, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

Organizational Relationships

Provide (for each applicant) an organizational chart containing the name and relationship of any person or entity who is related (as defined in Part 1130.140). If the related person or entity is participating in the development or funding of the project, describe the interest and the amount and type of any financial contribution.

APPEND DOCUMENTATION AS ATTACHMENT 4, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

Flood Plain Requirements [Refer to application instructions.]

Provide documentation that the project complies with the requirements of Illinois Executive Order #2006-5 pertaining to construction activities in special flood hazard areas. As part of the flood plain requirements, please provide a map of the proposed project location showing any identified floodplain areas. Floodplain maps can be printed at **www.FEMA.gov** or **www.illinoisfloodmaps.org**. **This map must be in a readable format**. In addition, please provide a statement attesting that the project complies with the requirements of Illinois Executive Order #2006-5 (http://www.hfsrb.illinois.gov). **NOTE:** A SPECIAL FLOOD HAZARD AREA AND 500-YEAR FLOODPLAIN DETERMINATION FORM has been added at the conclusion of this Application for Permit that must be completed to deem a project complete.

APPEND DOCUMENTATION AS ATTACHMENT 5, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

Historic Resources Preservation Act Requirements [Refer to application instructions.]

Provide documentation regarding compliance with the requirements of the Historic Resources Preservation Act.

APPEND DOCUMENTATION AS ATTACHMENT 6, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

DESCRIPTION OF PROJECT

1. Project Classification

[Check those applicable - refer to Part 1110.20 and Part 1120.20(b)]

Part 1110 Classification :

☐ Substantive

☒ Non-substantive

2. Narrative Description

In the space below, provide a brief narrative description of the project. Explain **WHAT** is to be done in **State Board defined terms**, **NOT WHY** it is being done. If the project site does NOT have a street address, include a legal description of the site. Include the rationale regarding the project's classification as substantive or non-substantive.

This Application is filed due to Modernization and Acquisition of Major Medical Equipment by UroPartners Imaging Center ("UroPartners") located at 2225 Enterprise Drive, Suite 3510, Westchester, IL 60154. Specifically, the Modernization by UroPartners includes the acquisition of major medical equipment pursuant to 77 Ill. Admin. Code 1110.270(a)(2)(c)(3)(A).

This major medical equipment includes a combined Positron Emission Tomography ("PET") and Computed Tomography ("CT") machine ("PET CT" machine), fixed artis ceiling (i.e., the mounting type of the Artis medical imaging system), mobile C-arm cios spin machine, maple ultrasound system, and other ancillary capital equipment. From a practical patient perspective, the operation of the lab will remain unchanged, with the same services being provided and the same physicians providing care post-acquisition of such equipment.

The above-described major medical equipment acquisition constitutes a non-substantive project, subject to review and approval by the Board.

Project Costs and Sources of Funds

Complete the following table listing all costs (refer to Part 1120.110) associated with the project. When a project or any component of a project is to be accomplished by lease, donation, gift, or other means, the fair market or dollar value (refer to Part 1130.140) of the component must be included in the estimated project cost. If the project contains non-reviewable components that are not related to the provision of health care, complete the second column of the table below. Note, the use and sources of funds must be equal.

Project Costs and Sources of Funds			
USE OF FUNDS	**CLINICAL**	**NONCLINICAL**	**TOTAL**
Preplanning Costs	-	-	-
Site Survey and Soil Investigation	-	-	-
Site Preparation	-	-	-
Off Site Work	-	-	-
New Construction Contracts	-	-	-
Modernization Contracts	$1,715,991	$807,525	$2,523,516
Contingencies	$170,000	$80,000	$250,000
Architectural/Engineering Fees	$148,620	$99,080	$247,700
Consulting and Other Fees	$100,000	$100,000	$200,000
Movable or Other Equipment (not in construction contracts)	$1,620,587	$762,629	$2,383,216
Bond Issuance Expense (project related)	-	-	-
Net Interest Expense During Construction (project related)	-	-	-
Fair Market Value of Leased Space or Equipment	-	-	-
Other Costs to Be Capitalized	$101,166	$47,608	$148,774
Acquisition of Building or Other Property (excluding land)	-	-	-
TOTAL USES OF FUNDS	$3,856,364	$1,896,842	$5,753,206
SOURCE OF FUNDS	**CLINICAL**	**NONCLINICAL**	**TOTAL**
Cash and Securities	$3,856,364	$1,896,842	$5,753,206
Pledges	0	0	0
Gifts and Bequests	0	0	0
Bond Issues (project related)	0	0	0
Mortgages	0	0	0
Leases (fair market value)	0	0	0
Governmental Appropriations	0	0	0
Grants	0	0	0
Other Funds and Sources	0	0	0
TOTAL SOURCES OF FUNDS	**$3,856,364**	**$1,896,842**	**$5,753,206**
NOTE: ITEMIZATION OF EACH LINE ITEM MUST BE PROVIDED AT ATTACHMENT 7, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.			

Related Project Costs

Provide the following information, as applicable, with respect to any land related to the project that will be or has been acquired during the last two calendar years:

Land acquisition is related to project ☐ Yes ☒ No
Purchase Price: $ N/A
Fair Market Value: $ N/A

The project involves the establishment of a new facility or a new category of service
☐ Yes ☒ No

If yes, provide the dollar amount of all **non-capitalized** operating start-up costs (including operating deficits) through the first full fiscal year when the project achieves or exceeds the target utilization specified in Part 1100.

Estimated start-up costs and operating deficit cost is $ N/A.

Project Status and Completion Schedules

For facilities in which prior permits have been issued please provide the permit numbers.

Indicate the stage of the project's architectural drawings:

☐ None or not applicable ☐ Preliminary
☒ Schematics ☐ Final Working

Anticipated project completion date (refer to Part 1130.140): July 1, 2026

Indicate the following with respect to project expenditures or to financial commitments (refer to Part 1130.140):

☐ Purchase orders, leases or contracts pertaining to the project have been executed. ☐ Financial commitment is contingent upon permit issuance. Provide a copy of the contingent "certification of financial commitment" document, highlighting any language related to CON Contingencies
☒ Financial Commitment will occur after permit issuance.

APPEND DOCUMENTATION AS ATTACHMENT 8, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

State Agency Submittals [Section 1130.620(c)]

Are the following submittals up to date as applicable?
☒ Cancer Registry
☒ APORS
☒ All formal document requests such as IDPH Questionnaires and Annual Bed Reports been submitted
☒ All reports regarding outstanding permits
Failure to be up to date with these requirements will result in the application for permit being deemed incomplete.

Cost Space Requirements

Provide in the following format, the **Departmental Gross Square Feet (DGSF)** or the **Building Gross Square Feet (BGSF)** and cost. The type of gross square footage either **DGSF** or **BGSF** must be identified. The sum of the department costs **MUST** equal the total estimated project costs. Indicate if any space is being reallocated for a different purpose. Include outside wall measurements plus the departments or area's portion of the surrounding circulation space. **Explain the use of any vacated space.**

Not Reviewable Space [i.e., non-clinical]: *means an area for the benefit of the patients, visitors, staff, or employees of a health care facility and not directly related to the diagnosis, treatment, or rehabilitation of persons receiving services from the health care facility. "Non-clinical service areas" include, but are not limited to, chapels; gift shops; newsstands; computer systems; tunnels, walkways, and elevators; telephone systems; projects to comply with life safety codes; educational facilities; student housing; patient, employee, staff, and visitor dining areas; administration and volunteer offices; modernization of structural components (such as roof replacement and masonry work); boiler repair or replacement; vehicle maintenance and storage facilities; parking facilities; mechanical systems for heating, ventilation, and air conditioning; loading docks; and repair or replacement of carpeting, tile, wall coverings, window coverings or treatments, or furniture. Solely for the purpose of this definition, "non-clinical service area" does not include health and fitness centers.* [20 ILCS 3960/3]

		Gross Square Feet		Amount of Proposed Total Gross Square Feet That Is:			
Dept. / Area	**Cost**	**Existing**	**Proposed**	**New Const.**	**Modernized**	**As Is**	**Vacated Space**
REVIEWABLE							
Diagnostic Radiology	$3,856,364		3,719	3,719			
Total Clinical	$3,856,364		3,719	3,719			
NON-REVIEWABLE							
Administrative	$1,896,842		1686	1686			
Total Non-clinical	$1,896,842		1686	1686			
TOTAL	**$5,753,206**		**5,405**	**5,405**			

APPEND DOCUMENTATION AS ATTACHMENT 9, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

Facility Bed Capacity and Utilization - NOT APPLICABLE

Complete the following chart, as applicable. Complete a separate chart for each facility that is a part of the project and insert the chart after this page. Provide the existing bed capacity and utilization data for the latest **Calendar Year for which data is available. Include observation days in the patient day totals for each bed service.** Any bed capacity discrepancy from the Inventory will result in the application being deemed **incomplete**.

FACILITY NAME: UroPartners Imaging Center			**CITY:** Westchester		
REPORTING PERIOD DATES:		**From: to:**			
Category of Service	**Operating Room**	**Number of Surgeries**	**Surgery Time (Hours)**	**Total Surgery Prep & Clean-Up Time (Hours)**	**Total Surgery Time (Hours)**
Medical/Surgical					
Obstetrics					
Pediatrics					
Intensive Care					
Comprehensive Physical Rehabilitation					
Acute/Chronic Mental Illness					
Neonatal Intensive Care					
General Long-Term Care					
Specialized Long-Term Care					
Long Term Acute Care					
Other (ASTC)					
TOTALS:					

CERTIFICATION

The Application must be signed by the authorized representatives of the applicant entity. Authorized representatives are:

- in the case of a corporation, any two of its officers or members of its Board of Directors.
- in the case of a limited liability company, any two of its managers or members (or the sole manager or member when two or more managers or members do not exist).
- in the case of a partnership, two of its general partners (or the sole general partner, when two or more general partners do not exist).
- in the case of estates and trusts, two of its beneficiaries (or the sole beneficiary when two or more beneficiaries do not exist); and
- in the case of a sole proprietor, the individual that is the proprietor.

**This Application is filed on the behalf of UroPartners, LLC *
in accordance with the requirements and procedures of the Illinois Health Facilities Planning Act. The undersigned certifies that he or she has the authority to execute and file this Application on behalf of the applicant entity. The undersigned further certifies that the data and information provided herein, and appended hereto, are complete and correct to the best of his or her knowledge and belief. The undersigned also certifies that the fee required for this application is sent herewith or will be paid upon request.**

SIGNATURE

GARY KIRSH
PRINTED NAME

CEO
PRINTED TITLE

Notarization:
Subscribed and sworn to before me
this 5th day of June 2025

Signature of Notary

Seal

MEGAN CRAIG
NOTARY PUBLIC
STATE OF OHIO
Comm. Expires
02-12-2029

SIGNATURE

DANIEL W. SCHARFF
PRINTED NAME

SECRETARY
PRINTED TITLE

Notarization:
Subscribed and sworn to before me
this 3rd day of June 2025

Signature of Notary

Seal

MEGAN CRAIG
NOTARY PUBLIC
STATE OF OHIO
Comm. Expires
02-12-2029

* Must be the EXACT legal name of the applicant

CERTIFICATION

The Application must be signed by the authorized representatives of the applicant entity. Authorized representatives are:

- in the case of a corporation, any two of its officers or members of its Board of Directors.
- in the case of a limited liability company, any two of its managers or members (or the sole manager or member when two or more managers or members do not exist).
- in the case of a partnership, two of its general partners (or the sole general partner, when two or more general partners do not exist).
- in the case of estates and trusts, two of its beneficiaries (or the sole beneficiary when two or more beneficiaries do not exist); and
- in the case of a sole proprietor, the individual that is the proprietor.

This Application is filed on the behalf of Solaris Health Holdings, LLC* **in accordance with the requirements and procedures of the Illinois Health Facilities Planning Act. The undersigned certifies that he or she has the authority to execute and file this Application on behalf of the applicant entity. The undersigned further certifies that the data and information provided herein, and appended hereto, are complete and correct to the best of his or her knowledge and belief. The undersigned also certifies that the fee required for this application is sent herewith or will be paid upon request.**

SIGNATURE

GARY M KIRSH

PRINTED NAME

CEO

PRINTED TITLE

Notarization:
Subscribed and sworn to before me
this 5th day of June 2025

Megan Craig

Signature of Notary

Seal

MEGAN CRAIG
NOTARY PUBLIC
STATE OF OHIO
Comm. Expires
02-12-2029

SIGNATURE

DANIEL W. SCHAAFF

PRINTED NAME

SECRETARY

PRINTED TITLE

Notarization:
Subscribed and sworn to before me
this 3rd day of June 2025

Megan Craig

Signature of Notary

Seal

MEGAN CRAIG
NOTARY PUBLIC
STATE OF OHIO
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*ACS legal name of the applicant

SECTION III. BACKGROUND, PURPOSE OF THE PROJECT, AND ALTERNATIVES - INFORMATION REQUIREMENTS

This Section is applicable to all projects except those that are solely for discontinuation with no project costs.

1110.110(a) – Background of the Applicant

READ THE REVIEW CRITERION and provide the following required information:

BACKGROUND OF APPLICANT

1. A listing of all health care facilities owned or operated by the applicant, including licensing, and certification if applicable.
2. A listing of all health care facilities currently owned and/or operated in Illinois, by any corporate officers or directors, LLC members, partners, or owners of at least 5% of the proposed health care facility.
3. For the following questions, please provide information for each applicant, including corporate officers or directors, LLC members, partners, and owners of at least 5% of the proposed facility. A health care facility is considered owned or operated by every person or entity that owns, directly or indirectly, an ownership interest.
    a. A certified listing of any adverse action taken against any facility owned and/or operated by the applicant, directly or indirectly, during the three years prior to the filing of the application.
    b. A certified listing of each applicant, identifying those individuals that have been cited, arrested, taken into custody, charged with, indicted, convicted, or tried for, or pled guilty to the commission of any felony or misdemeanor or violation of the law, except for minor parking violations; or the subject of any juvenile delinquency or youthful offender proceeding. Unless expunged, provide details about the conviction, and submit any police or court records regarding any matters disclosed.
    c. A certified and detailed listing of each applicant or person charged with fraudulent conduct or any act involving moral turpitude.
    d. A certified listing of each applicant with one or more unsatisfied judgements against him or her.
    e. A certified and detailed listing of each applicant who is in default in the performance or discharge of any duty or obligation imposed by a judgment, decree, order or directive of any court or governmental agency.
4. Authorization permitting HFSRB and DPH access to any documents necessary to verify the information submitted, including, but not limited to official records of DPH or other State agencies; the licensing or certification records of other states, when applicable; and the records of nationally recognized accreditation organizations. **Failure to provide such authorization shall constitute an abandonment or withdrawal of the application without any further action by HFSRB.**
5. If, during a given calendar year, an applicant submits more than one application for permit, the documentation provided with the prior applications may be utilized to fulfill the information requirements of this criterion. In such instances, the applicant shall attest that the information was previously provided, cite the project number of the prior application, and certify that no changes have occurred regarding the information that has been previously provided. The applicant can submit amendments to previously submitted information, as needed, to update and/or clarify data.

APPEND DOCUMENTATION AS ATTACHMENT 11, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM. EACH ITEM (1-4) MUST BE IDENTIFIED IN ATTACHMENT 11.

Criterion 1110.110(b) & (d)

PURPOSE OF PROJECT

1. Document that the project will provide health services that improve the health care or well-being of the market area population to be served.
2. Define the planning area or market area, or other relevant area, per the applicant's definition.
3. Identify the existing problems or issues that need to be addressed as applicable and appropriate for the project.
4. Cite the sources of the documentation.
5. Detail how the project will address or improve the previously referenced issues, as well as the population's health status and well-being.
6. Provide goals with quantified and measurable objectives, with specific timeframes that relate to achieving the stated goals **as appropriate**.

For projects involving modernization, describe the conditions being upgraded, if any. For facility projects, include statements of the age and condition of the project site, as well as regulatory citations, if any. For equipment being replaced, include repair and maintenance records.

NOTE: Information regarding the "Purpose of the Project" will be included in the State Board Staff Report.

APPEND DOCUMENTATION AS ATTACHMENT 12, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM. EACH ITEM (1-6) MUST BE IDENTIFIED IN ATTACHMENT 12.

ALTERNATIVES

1) Identify **ALL** the alternatives to the proposed project:

   Alternative options **must** include:

   A) Proposing a project of greater or lesser scope and cost.

   B) Pursuing a joint venture or similar arrangement with one or more providers or entities to meet all or a portion of the project's intended purposes; developing alternative settings to meet all or a portion of the project's intended purposes.

   C) Utilizing other health care resources that are available to serve all or a portion of the population proposed to be served by the project; and

   D) Provide the reasons why the chosen alternative was selected.

2) Documentation shall consist of a comparison of the project to alternative options. The comparison shall address issues of total costs, patient access, quality, and financial benefits in both the short-term (within one to three years after project completion) and long-term. This may vary by project or situation. **FOR EVERY ALTERNATIVE IDENTIFIED, THE TOTAL PROJECT COST AND THE REASONS WHY THE ALTERNATIVE WAS REJECTED MUST BE PROVIDED.**

3) The applicant shall provide empirical evidence, including quantified outcome data that verifies improved quality of care, as available.

APPEND DOCUMENTATION AS ATTACHMENT 13, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

SECTION IV. PROJECT SCOPE, UTILIZATION, AND UNFINISHED/SHELL SPACE

Criterion 1110.120 - Project Scope, Utilization, and Unfinished/Shell Space

READ THE REVIEW CRITERION and provide the following information:

SIZE OF PROJECT:

1. Document that the amount of physical space proposed for the proposed project is necessary and not excessive. **This must be a narrative and it shall include the basis used for determining the space and the methodology applied.**
2. If the gross square footage exceeds the BGSF/DGSF standards in Appendix B, justify the discrepancy by documenting one of the following:
    a. Additional space is needed due to the scope of services provided, justified by clinical or operational needs, as supported by published data or studies and certified by the facility's Medical Director.
    b. The existing facility's physical configuration has constraints or impediments and requires an architectural design that delineates the constraints or impediments.
    c. The project involves the conversion of existing space that results in excess square footage.
    d. Additional space is mandated by governmental or certification agency requirements that were not in existence when Appendix B standards were adopted.

Provide a narrative for any discrepancies from the State Standard. A table must be provided in the following format with Attachment 14.

SIZE OF PROJECT				
DEPARTMENT / SERVICE	**PROPOSED BGSF/DGSF**	**STATE STANDARD**	**DIFFERENCE**	**MET STANDARD?**
Diagnostic Radiology (Ultrasound, PET CT Machine,)	**464 GSF** Ultrasound Machine is mobile and not fixed equipment	**Total: 2,700 GSF** 1,800 GSF Per Unit (PET Scan); 900 GSF Per Unit (Ultrasound)	**2,236 GSF**	**YES**

APPEND DOCUMENTATION AS ATTACHMENT 14, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

PROJECT SERVICES UTILIZATION:

This criterion is applicable only to projects or portions of projects that involve services, functions, or equipment for which HFSRB has established utilization standards or occupancy targets in 77 Ill. Adm. Code 1100.

Document that in the second year of operation, the annual utilization of the service or equipment shall meet or exceed the utilization standards specified in 1110.Appendix B. **A narrative of the rationale that supports the projections must be provided.**

A table must be provided in the following format with Attachment 15.

UTILIZATION					
	DEPARTMENT / SERVICE	**HISTORICAL UTILIZATION (PATIENT DAYS) (TREATMENTS) ETC.**	**PROJECTED UTILIZATION**	**STATE STANDARD**	**MEET STANDARD?**
YEAR 1	**PET CT Scan** **Ultrasound**	**3,180** **3,180**	**3,180** **3,180**	**3,600** **3,100**	**YES**
YEAR 2	**PET CT Scan** **Ultrasound**	**3,180** **3,180**	**3,339** **3,339**	**3,600** **3,100**	**YES**

APPEND DOCUMENTATION AS ATTACHMENT 15, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

UNFINISHED OR SHELL SPACE:

Provide the following information:

1. Total gross square footage (GSF) of the proposed shell space.
2. The anticipated use of the shell space, specifying the proposed GSF to be allocated to each department, area, or function.
3. Evidence that the shell space is being constructed due to:
    a. Requirements of governmental or certification agencies; or
    b. Experienced increases in the historical occupancy or utilization of those areas proposed to occupy the shell space.
4. Provide:
    a. Historical utilization for the area for the latest five-year period for which data is available; and
    b. Based upon the average annual percentage increase for that period, projections of future utilization of the area through the anticipated date when the shell space will be placed into operation.

APPEND DOCUMENTATION AS ATTACHMENT 16, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

ASSURANCES:

Submit the following:

1. Verification that the applicant will submit to HFSRB a CON application to develop and utilize the shell space, regardless of the capital thresholds in effect at the time or the categories of service involved.
2. The estimated date by which the subsequent CON application (to develop and utilize the subject shell space) will be submitted; and
3. The anticipated date when the shell space will be completed and placed into operation.

APPEND DOCUMENTATION AS ATTACHMENT 17, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

M. Criterion 1110.270 - Clinical Service Areas Other than Categories of Service

1. Applicants proposing to establish, expand and/or modernize Clinical Service Areas Other than categories of service must submit the following information:

2. Indicate changes by Service: Indicate # of key room changes by action(s):

Service	# Existing Key Rooms	# Proposed Key Rooms
☒ **Ultrasound**	1	1
☒ **PET Scan**	1	1
☐		

3. READ the applicable review criteria outlined below and **submit the required documentation for the criteria:**

Project Type	Required Review Criteria
New Services or Facility or Equipment	**(b) – Need Determination – Establishment**
Service Modernization	(c)(1) – Deteriorated Facilities
	AND/OR
	(c)(2) – Necessary Expansion
	PLUS
	(c)(3)(A) – Utilization – Major Medical Equipment
	OR
	(c)(3)(B) – Utilization – Service or Facility
1APPEND DOCUMENTATION AS ATTACHMENT 31, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.	

The following Sections DO NOT need to be addressed by the applicants or co-applicants responsible for funding or guaranteeing the funding of the project if the applicant has a bond rating of A- or better from Fitch's or Standard and Poor's rating agencies, or A3 or better from Moody's (the rating shall be affirmed within the latest 18-month period prior to the submittal of the application):

- **Section 1120.120 Availability of Funds – Review Criteria**
- **Section 1120.130 Financial Viability – Review Criteria**
- **Section 1120.140 Economic Feasibility – Review Criteria, subsection (a)**

SECTION VII. 1120.120 - AVAILABILITY OF FUNDS

The applicant shall document those financial resources shall be available and be equal to or exceed the estimated total project cost plus any related project costs by providing evidence of sufficient financial resources from the following sources, as applicable **[Indicate the dollar amount to be provided from the following sources]:**

$5,753,206	a) Cash and Securities – statements (e.g., audited financial statements, letters from financial institutions, board resolutions) as to: 1) the amount of cash and securities available for the project, including the identification of any security, its value and availability of such funds; and 2) interest to be earned on depreciation account funds or to be earned on any asset from the date of applicant's submission through project completion.
_____	b) Pledges – for anticipated pledges, a summary of the anticipated pledges showing anticipated receipts and discounted value, estimated timetable of gross receipts and related fundraising expenses, and a discussion of past fundraising experience.
_____	c) Gifts and Bequests – verification of the dollar amount, identification of any conditions of use, and the estimated timetable of receipts.
_____	d) Debt – a statement of the estimated terms and conditions (including the debt time, variable or permanent interest rates over the debt time, and the anticipated repayment schedule) for any interim and for the permanent financing proposed to fund the project, including: 1) For general obligation bonds, proof of passage of the required referendum or evidence that the governmental unit has the authority to issue the bonds and evidence of the dollar amount of the issue, including any discounting anticipated. 2) For revenue bonds, proof of the feasibility of securing the specified amount and interest rate. 3) For mortgages, a letter from the prospective lender attesting to the expectation of making the loan in the amount and time indicated, including the anticipated interest rate and any conditions associated with the mortgage, such as, but not limited to, adjustable interest rates, balloon payments, etc. 4) For any lease, a copy of the lease, including all the terms and conditions, including any purchase options, any capital improvements to the property and provision of capital equipment. 5) For any option to lease, a copy of the option, including all terms and conditions.
_____	e) Governmental Appropriations – a copy of the appropriation Act or ordinance accompanied by a statement of funding availability from an official of the governmental unit. If funds are to be made available from subsequent fiscal years, a copy of a resolution or other action of the governmental unit attesting to this intent.
_____	f) Grants – a letter from the granting agency as to the availability of funds in terms of the amount and time of receipt.
_____	g) All Other Funds and Sources – verification of the amount and type of any other funds that will be used for the project.
$5,753,206	**TOTAL FUNDS AVAILABLE**

APPEND DOCUMENTATION AS ATTACHMENT 34, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

SECTION VIII. 1120.130 - FINANCIAL VIABILITY- WAIVER MET

All the applicants and co-applicants shall be identified, specifying their roles in the project funding, or guaranteeing the funding (sole responsibility or shared) and percentage of participation in that funding.

Financial Viability Waiver

The applicant is not required to submit financial viability ratios if:

1. "A" Bond rating or better
2. **All the project's capital expenditures are completely funded through internal sources**
3. The applicant's current debt financing or projected debt financing is insured or anticipated to be insured by MBIA (Municipal Bond Insurance Association Inc.) or equivalent
4. The applicant provides a third-party surety bond or performance bond letter of credit from an A rated guarantor.

See Section 1120.130 Financial Waiver for information to be provided

APPEND DOCUMENTATION AS ATTACHMENT 35, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

The applicant or co-applicant that is responsible for funding or guaranteeing funding of the project shall provide viability ratios for the latest three years for which **audited financial statements are available and for the first full fiscal year at target utilization, but no more than two years following project completion.** When the applicant's facility does not have facility specific financial statements and the facility is a member of a health care system that has combined or consolidated financial statements, the system's viability ratios shall be provided. If the health care system includes one or more hospitals, the system's viability ratios shall be evaluated for conformance with the applicable hospital standards.

	Historical 3 Years			Projected
Enter Historical and/or Projected Years:				
Current Ratio				
Net Margin Percentage				
Percent Debt to Total Capitalization				
Projected Debt Service Coverage				
Days Cash on Hand				
Cushion Ratio				

Provide the methodology and worksheets utilized in determining the ratios detailing the calculation and applicable line item amounts from the financial statements. Complete a separate table for each co-applicant and provide worksheets for each.

Variance

Applicants not in compliance with any of the viability ratios shall document that another organization, public or private, shall assume the legal responsibility to meet the debt obligations should the applicant default.

APPEND DOCUMENTATION AS ATTACHMENT 36, IN NUMERICAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

SECTION IX. 1120.140 - ECONOMIC FEASIBILITY

This section is applicable to all projects subject to Part 1120.

A. Reasonableness of Financing Arrangements

The applicant shall document the reasonableness of financing arrangements by submitting a notarized statement signed by an authorized representative that attests to one of the following:

1) That the total estimated project costs and related costs will be funded in total with cash and equivalents, including investment securities, unrestricted funds, received pledge receipts and funded depreciation; or

2) That the total estimated project costs and related costs will be funded in total or in part by borrowing because:

   A) A portion or all the cash and equivalents must be retained in the balance sheet asset accounts to maintain a current ratio of at least 2.0 times for hospitals and 1.5 times for all other facilities; or

   B) Borrowing is less costly than the liquidation of existing investments, and the existing investments being retained may be converted to cash or used to retire debt within a 60-day period.

B. Conditions of Debt Financing

This criterion is applicable only to projects that involve debt financing. The applicant shall document that the conditions of debt financing are reasonable by submitting a notarized statement signed by an authorized representative that attests to the following, as applicable:

1) That the selected form of debt financing for the project will be at the lowest net cost available.

2) That the selected form of debt financing will not be at the lowest net cost available but is more advantageous due to such terms as prepayment privileges, no required mortgage, access to additional indebtedness, term (years), financing costs and other factors.

3) That the project involves (in total or in part) the leasing of equipment or facilities and that the expenses incurred with leasing a facility or equipment are less costly than constructing a new facility or purchasing new equipment.

C. Reasonableness of Project and Related Costs

Read the criterion and provide the following:

1) Identify each department or area impacted by the proposed project and provide a cost and square footage allocation for new construction and/or modernization using the following format (insert after this page).

COST AND GROSS SQUARE FEET BY DEPARTMENT OR SERVICE

Department (List below)	A	B	C	D	E	F	G	H	Total Cost (G + H)
	Cost/Square Foot New	Cost/Square Foot Mod.	Gross Sq. Ft. New Circ.*		Gross Sq. Ft. Mod.	Circ.*	Const. $ (A x C)	Mod. $ (B x E)	
Diagnostic Equipment (Ultrasound and PET CT Scan)		$461.41			3,719			$1,715,991	$1,715,991
Contingency		$45.71			3,719			$170,000	$170,000
TOTALS		$507.12			3,719			$1,885,991	$1,885,991

* Include the percentage (%) of space for circulation

D. Projected Operating Costs

The applicant shall provide the projected direct annual operating costs (in current dollars per equivalent patient day or unit of service) for the first full fiscal year at target utilization but no more than two years following project completion. Direct cost means the fully allocated costs of salaries, benefits and supplies for the service.

E. Total Effect of the Project on Capital Costs

The applicant shall provide the total projected annual capital costs (in current dollars per equivalent patient day) for the first full fiscal year at target utilization but no more than two years following project completion.

APPEND DOCUMENTATION AS ATTACHMENT 37, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

SECTION X. SAFETY NET IMPACT STATEMENT

SAFETY NET IMPACT STATEMENT that describes all the following must be submitted for ALL SUBSTANTIVE PROJECTS AND PROJECTS TO DISCONTINUE HEALTH CARE FACILITIES [20 ILCS 3960/5.4]:

1. The project's material impact, if any, on essential safety net services in the community, ***including the impact on racial and health care disparities in the community,*** to the extent that it is feasible for an applicant to have such knowledge.

2. The project's impact on the ability of another provider or health care system to cross-subsidize safety net services, if reasonably known to the applicant.

3. How the discontinuation of a facility or service might impact the remaining safety net providers in each community, if reasonably known by the applicant.

Safety Net Impact Statements shall also include all the following:

1. For the 3 fiscal years prior to the application, a certification describing the amount of charity care provided by the applicant. The amount calculated by hospital applicants shall be in accordance with the reporting requirements for charity care reporting in the Illinois Community Benefits Act. Non-hospital applicants shall report charity care, at cost, in accordance with an appropriate methodology specified by the Board.

2. For the 3 fiscal years prior to the application, a certification of the amount of care provided to Medicaid patients. Hospital and non-hospital applicants shall provide Medicaid information in a manner consistent with the information reported each year to the Illinois Department of Public Health regarding "Inpatients and Outpatients Served by Payor Source" and "Inpatient and Outpatient Net Revenue by Payor Source" as required by the Board under Section 13 of this Act and published in the Annual Hospital Profile.

3. Any information the applicant believes is directly relevant to safety net services, including information regarding teaching, research, and any other service.

A table in the following format must be provided as part of Attachment 37.

Safety Net Information per PA 96-0031			
CHARITY CARE			
Charity (# of patients)	**2020**	**2021**	**2022**
Inpatient	-	-	-
Outpatient	-	-	-
Total	-	-	-
Charity (cost in dollars)			
Inpatient	-	-	-
Outpatient	-	-	-
Total	-	-	-
MEDICAID			
Medicaid (# of patients)	**2020**	**2021**	**2022**
Inpatient	-	-	-
Outpatient	-	-	-
Total	-	-	-
Medicaid (revenue)			
Inpatient	-	-	-
Outpatient	-	-	-
Total	-	-	-

APPEND DOCUMENTATION AS ATTACHMENT 38, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

SECTION X. CHARITY CARE INFORMATION

Charity Care information MUST be furnished for ALL projects [1120.20(c)].

1. All applicants and co-applicants shall indicate the amount of charity care for the latest three **audited** fiscal years, the cost of charity care and the ratio of that charity care cost to net patient revenue.
2. If the applicant owns or operates one or more facilities, the reporting shall be for each individual facility located in Illinois. If charity care costs are reported on a consolidated basis, the applicant shall provide documentation as to the cost of charity care; the ratio of that charity care to the net patient revenue for the consolidated financial statement; the allocation of charity care costs; and the ratio of charity care cost to net patient revenue for the facility under review.
3. If the applicant is not an existing facility, it shall submit the facility's projected patient mix by payer source, anticipated charity care expense and projected ratio of charity care to net patient revenue by the end of its second year of operation.

Charity care" means care provided by a health care facility for which the provider does not expect to receive payment from the patient or a third-party payer (20 ILCS 3960/3). Charity Care must be provided at cost.

A table in the following format must be provided for all facilities as part of Attachment 39.

CHARITY CARE			
	2020	2021	2022
Net Patient Revenue	-	-	-
Amount of Charity Care (charges)	-	-	-
Cost of Charity Care	-	-	-

APPEND DOCUMENTATION AS ATTACHMENT 39, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

SECTION XI. SPECIAL FLOOD HAZARD AREA AND 500-YEAR FLOODPLAIN DETERMINATION FORM

In accordance with Executive Order 2006-5 (EO 5), the Health Facilities & Services Review Board (HFSRB) must determine if the site of the CRITICAL FACILITY, as defined in EO 5, is in a mapped floodplain (Special Flood Hazard Area) or a 500-year floodplain. All state agencies are required to ensure that before a permit, grant or a development is planned or promoted, the proposed project meets the requirements of the Executive Order, including compliance with the National Flood Insurance Program (NFIP) and state floodplain regulation.

1. Applicant: UroPartners Imaging Center (Name) 2225 Enterprise Drive, Suite 3510 (Address)

Westchester (City) IL (State) 60154 (ZIP Code) (708) 486-0076 (Telephone Number)

2. Project Location: 2225 Enterprise Drive, Suite 3510 (Address) Westchester (City) IL (State)

Cook (County) Proviso (Township) 30 (Section)

3. You can create a small map of your site showing the FEMA floodplain mapping using the FEMA Map Service Center website (https://msc.fema.gov/portal/home) by entering the address for the property in the Search bar. If a map, like that shown on page 2 is shown, select the ***Go to NFHL Viewer*** tab above the map. You can print a copy of the floodplain map by selecting the  icon in the top corner of the page. Select the pin tool icon  and place a pin on your site. Print a FIRMETTE size image.
If there is no digital floodplain map available select the **View/Print FIRM** icon above the aerial photo. You will then need to use the Zoom tools provided to locate the property on the map and use the **Make a FIRMette** tool to create a pdf of the floodplain map.

IS THE PROJECT SITE LOCATED IN A SPECIAL FLOOD HAZARD AREA: Yes___ No _X_

IS THE PROJECT SITE LOCATED IN THE 500-YEAR FLOOD PLAIN? NO

If you are unable to determine if the site is in the mapped floodplain or 500-year floodplain, contact the county or the local community building or planning department for assistance.

If the determination is being made by a local official, please complete the following:

FIRM Panel Number:_____ Effective Date: _____

Name of Official:_____ Title: _____

Business/Agency: _____ Address: _____

_____
(City) (State) (ZIP Code) (Telephone Number)

Signature: _____ Date: _____

NOTE: This finding only means that the property in question is or is not in a Special Flood Hazard Area or a 500-year floodplain as designated on the map noted above. It does not constitute a guarantee that the property will or will not be flooded or be subject to local drainage problems.

If you need additional help, contact the Illinois Statewide Floodplain Program at 217/782-4428

After paginating the entire completed application indicate, in the chart below, the page numbers for the included attachments:

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	SERVICE SPECIFIC:	
18	Medical Surgical Pediatrics, Obstetrics, ICU	N/A
19	Comprehensive Physical Rehabilitation	N/A
20	Acute Mental Illness	N/A
21	Open Heart Surgery	N/A
22	Cardiac Catheterization	N/A
23	In-Center Hemodialysis	N/A
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ATTACHMENT 1
Certificate of Good Standing

Included with this attachment are the Certificates of Good Standing for:

1. UroPartners, LLC; and
2. Solaris Health Holdings, LLC.

ATTACHMENT 1
Certificate of Good Standing - UroPartners, LLC

File Number 0142447-5

STATE OF ILLINOIS
OFFICE OF
THE SECRETARY OF STATE

To all to whom these Presents Shall Come, Greeting:

I, **Alexi Giannoulias,** *Secretary of State of the State of Illinois, do hereby certify that I am the keeper of the records of the Department of Business Services. I certify that*

UROPARTNERS, LLC, HAVING ORGANIZED IN THE STATE OF ILLINOIS ON FEBRUARY 10, 2005, APPEARS TO HAVE COMPLIED WITH ALL PROVISIONS OF THE LIMITED LIABILITY COMPANY ACT OF THIS STATE, AND AS OF THIS DATE IS IN GOOD STANDING AS A DOMESTIC LIMITED LIABILITY COMPANY IN THE STATE OF ILLINOIS.

In Testimony Whereof, *I hereto set my hand and cause to be affixed the Great Seal of the State of Illinois, this* 31ST *day of* MARCH *A.D.* 2025 .

Authentication #: 2509004334 verifiable until 03/31/2026
Authenticate at: https://www.ilsos.gov

SECRETARY OF STATE

ATTACHMENT 1
Certificate of Good Standing – Solaris Health Holdings, LLC

File Number 0946194-9

STATE OF ILLINOIS
OFFICE OF
THE SECRETARY OF STATE

To all to whom these Presents Shall Come, Greeting:

I, Alexi Giannoulias, *Secretary of State of the State of Illinois, do hereby certify that I am the keeper of the records of the Department of Business Services. I certify that*

SOLARIS HEALTH HOLDINGS, LLC, A DELAWARE LIMITED LIABILITY COMPANY HAVING OBTAINED ADMISSION TO TRANSACT BUSINESS IN ILLINOIS ON FEBRUARY 23, 2021, APPEARS TO HAVE COMPLIED WITH ALL PROVISIONS OF THE LIMITED LIABILITY COMPANY ACT OF THIS STATE, AND AS OF THIS DATE IS IN GOOD STANDING AS A FOREIGN LIMITED LIABILITY COMPANY ADMITTED TO TRANSACT BUSINESS IN THE STATE OF ILLINOIS.

In Testimony Whereof, *I hereto set my hand and cause to be affixed the Great Seal of the State of Illinois, this* 31ST *day of* MARCH *A.D.* 2025 .

SEAL OF THE STATE OF ILLINOIS
AUG. 26TH 1818

Authentication #: 2509004348 verifiable until 03/31/2026
Authenticate at: https://www.ilsos.gov

SECRETARY OF STATE

ATTACHMENT 2
Site Ownership

The Imaging Center lease will remain with Solaris Health Holdings, LLC, following the modernization and acquisition of medical equipment. There will be no transfer of land ownership. Attached as evidence is a copy of the office building lease agreements and the office building assignment of lease consent.

ATTACHMENT 2
Site Ownership

TWELFTH AMENDMENT TO LEASE

This Twelfth Amendment to Lease ("Twelfth Amendment"), dated this 31st day of January, 2025, is by and between **ENTERPRISE CENTRE LLC**, an Illinois limited **liability company, ("Landlord"), and SOLARIS HEALTH HOLDINGS, LLC**, a Delaware **limited liability company ("Tenant").**

RECITALS

A. WHEREAS, UROPARTNERS, LLC, an Illinois limited liability company **("SubTenant") and Landlord entered into an Office Building Lease dated August 15, 2005,** a First Amendment to Lease dated November 11, 2005, a Second Amendment to Lease dated April 19, 2006, a Third Amendment to Lease dated October 6, 2006, a Fourth Amendment to Lease dated March 7, 2008, a Fifth Amendment to Lease dated April 23, 2009, a Sixth Amendment to Lease dated October 23, 2009 a Seventh Amendment to Lease dated October 5, 2011, an Eighth Amendment to Lease dated April 7, 2015, a Commencement Letter dated November 7, 2016, a Ninth Amendment to Lease dated April 16, 2018, a Commencement Letter dated July 12, 2018, a Tenth Amendment to Lease dated January 22, 2020, a commencement Letter dated May 28, 2020, and an Eleventh Amendment to Lease dated September 2023 (collectively, the "Lease") pursuant to which SubTenant leased Suites 2508, 2511, 2513 and 2514 (collectively, the **"25 Building Premises"), and Suites 4502, 4504, 4506, and 4512 (collectively, the "45 Building Premises"), the 25 Building Premises and the 45 Building Premises are hereinafter collectively referred to as the "Premises" at 2225 Enterprise Drive,** Westchester, Illinois 60154, (the "Building") located at the property commonly known as Enterprise Center, 2205 **– 2255 Enterprise Drive (the "Complex"); and**

B. WHEREAS, pursuant to the terms of the Eleventh Amendment to Lease, SubTenant subsequently assigned the Lease to Tenant and Tenant assumed all liabilities and obligations of SubTenant under the Lease with SubTenant remaining fully liable under the Lease; and

C. WHEREAS, Tenant subsequently subleased all of the Premises at the Building to SubTenant; and

D. WHEREAS, as of the date of this Twelfth Amendment, the Premises contains 18,448 rentable square feet; and

E. WHEREAS, Landlord and Tenant now desire to make certain further amendments to the Lease as contained herein.

NOW THEREFORE, in consideration of the mutual promises contained herein, and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Landlord and Tenant agree as follows:

ATTACHMENT 2
Site Ownership

1. This Twelfth Amendment to Lease is hereby attached to and made part of the Lease and is specifically incorporated into the Lease. Except as otherwise expressly indicated herein, all capitalized terms shall have the meanings ascribed to them in the Lease. To the extent any terms and provisions of this Twelfth Amendment are inconsistent with the terms and provisions of the Lease, the terms and provisions of this Twelfth Amendment shall prevail. Except as amended herein, the Lease shall remain in full force and effect in accordance with its terms through the entire term of the Lease, as amended.

2. This Twelfth Amendment to Lease is not intended to modify or affect the Lease in any way whatsoever except as expressly provided for in this Twelfth Amendment. The parties hereby confirm that the Lease, as amended by this Twelfth Amendment, is in full force and effect. To the best of Tenant's knowledge, Landlord is not in default under the Lease.

3. LEASE TERM: Effective upon the execution hereof, the Term of the Lease with respect to the Expansion Space (hereinafter defined) shall be from the date of delivery of the Expansion Space to Tenant through the one hundred thirtieth (130th) full calendar month after the Expansion Rent Commencement Date (hereinafter defined), **hereinafter referred to as, the "Expansion Expiration Date". Such** period from the date of execution hereof through the Expansion Expiration Date shall be referred to as, the **"Amended Term".**

4. EXPANSION SPACE: Tenant agrees to lease and expand the Premises to include Suite 3510 and Suite 3501 in the 2235 Enterprise Drive **Building (the "35 Building")** consisting of approximately 4,569 and 1,700 rentable square feet respectively (the **"Expansion Space"). The Expansion Space is shown on Exhibit A attached hereto. Tenant** shall be granted possession of said Expansion Space on the following terms and conditions:

A. LEASE OF ADDITIONAL SPACE: In addition to the Premises **currently leased by Tenant under the Lease, (the "Current Space") and effective** upon complete execution hereof, and delivery of the Expansion Space to Tenant, Landlord leases to Tenant, and Tenant accepts, the Expansion Space. The Expansion Space and the Current Space are hereinafter cumulatively referred to as the "Total Space." The rentable square footage of the Total Space shall be 24,717 rentable square feet.

B. CONDITION OF EXPANSION SPACE: No Landlord Work. The Tenant's taking possession of the Expansion Space shall be conclusive evidence that the Expansion Space and the Building were in good order and satisfactory condition when the Tenant took possession, and Tenant, having examined the Expansion Space, accepts same in "AS-IS" condition. No promise of the Landlord to alter, remodel or improve the Expansion Space or the Building and no representation respecting the condition of the Expansion Space or the Building have been made by the Landlord to the Tenant.

ATTACHMENT 2
Site Ownership

(i). Tenant's Work. Tenant shall, at its sole cost and expense, subject to Landlord's Allowance as hereinbelow defined, "build-out" the Expansion Space for its intended use using a general contractor of its choice ("Tenant's Work"). Tenant's Work performed by Tenant shall be made in full accordance with the plans and specifications approved by Landlord, not to be unreasonably withheld, conditioned or delayed. No building permits for any Tenant's Work shall be applied for until the applications therefore have been submitted to and approved in writing by Landlord, not to be unreasonably withheld, conditioned or delayed. No work shall be commenced in connection with any of Tenant's Work or any subsequent alterations or additions to the Expansion Space desired by Tenant until (i) the plans, specifications and contract(s) to be entered into by Tenant pertaining to such alterations or additions have been submitted to and approved in writing by Landlord, not to be unreasonably withheld, conditioned or delayed. Any such plans produced by Landlord or Landlord's agents are hereby approved. The approval of the Landlord of such third party produced plans and specifications shall not constitute the assumption of any liability on the part of Landlord for their accuracy or their conformity with Building Code requirements, and Tenant shall be solely responsible for such plans. The approval of Tenant's third party produced plans and specifications shall not constitute a waiver by Landlord of the right to thereafter require Tenant to amend the same to provide for omissions therein later discovered by Landlord; and (ii) Tenant or its contractor shall have deposited with Landlord certificates of an insurance policy or policies in an amount satisfactory to Landlord and issued by a company or companies approved by Landlord, indemnifying Landlord against any and all claims of every kind, because of accident, injury or damage to any person or property arising out of the work done in connection with the making of such alterations. The general contractor selected by Tenant shall provide Workers' Compensation insurance and evidence same to Landlord.

Every person who furnishes labor or services, or who is in any way connected with any and all repairs, replacements, alterations, improvements or changes made by or at the instance of Tenant in or to the Premises, the fixtures or equipment in connection therewith, or the appurtenances thereto belonging shall, prior to commencement of any such work, furnish Landlord with sworn contractors' statements. No payment shall be made to any such person unless Landlord is furnished with and approves waivers of lien against any mechanic's lien in connection with said improvements, alterations or additions.

Tenant shall take all other steps necessary to ensure that no liens attach to the Building by virtue of any work performed or materials or equipment installed on Tenant's behalf, and Tenant expressly warrants to Landlord that no such liens shall attach.

All Tenant's Work shall be performed in a good, workmanlike, and professional manner.

(ii) Landlord's Allowance. Tenant shall, at Landlord's sole cost and expense up to Three Hundred Ninety-Nine Thousand Five Hundred Eight-Six and 00/100 Dollars ($399,586.00, "Landlord's Allowance") and thereafter at Tenant's sole cost and

ATTACHMENT 2
Site Ownership

expense, perform Tenant's Work pursuant to the Lease. The full cost of Tenant's Work shall be paid by Landlord to Tenant or Tenant's contractor (the "Contractor").

Tenant may submit draw requests, no more than once every thirty (30) days, which request must include a certificate stating that the amount of the Landlord Allowance then being requested represents amounts paid by Tenant on account of Tenant's Work to contractors, subcontractors, materialmen, engineers, architects or other persons who have rendered or furnished services or materials for the work and giving a brief description of such services and materials and the several amounts so paid to each of such persons with respect thereto (however, in any case, such request shall not exceed a pro-rata share based on the total construction contract executed by Tenant) and Tenant shall deliver to Landlord partial or final waivers of lien (as appropriate) from such contractors subcontractors, materialmen, engineers, architects or other persons who have rendered or furnished services or materials for work. Payment of such amount requested shall be due within thirty (30) days of Landlord's receipt of Landlord's notice of approval of each such Tenant draw request.

C. BASE RENT: Effective as of the earlier of (i) Tenant opening for business in the Premises; (ii) ten (10) business days after substantial completion of Tenant's Work and issuance of an occupancy certificate (or equivalent) by the Village of Westchester; and (iii) three hundred (300) days following the date hereof (the "Expansion Rent Commencement Date", or "Expansion RCD") with respect to the Expansion Space only, Tenant shall pay to Landlord at the office of Landlord or at such other place as Landlord may designate, in writing to Tenant, monthly Base Rent during the Amended Term as follows:

Period	Monthly Base Rent
Expansion RCD through September 30, 2026	$11,704.00
October 1, 2026 through September 30, 2027	$12,142.00
October 1, 2027 through September 30, 2028	$12,598.00
October 1, 2028 through September 30, 2029	$13,073.00
October 1, 2029 through September 30, 2030	$13,566.00
October 1, 2030 through September 30, 2031	$14,079.00
October 1, 2031 through September 30, 2032	$14,613.00
October 1, 2032 through September 30, 2033	$15,167.00
October 1, 2033 through September 30, 2034	$15,744.00
October 1, 2034 through Expiration Date	$16,345.00

Notwithstanding anything to the contrary contained herein, so long as Tenant is not then in default under any of the terms, conditions or obligations of the Lease after any applicable cure and grace periods, monthly Base Rent for the Expansion Space only shall abate for the

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following five (5) months of the Amended Term: the 67th, 79th, 91st, 103rd, and 115th full calendar months after the Expansion Rent Commencement Date.

5. OPTION TO TERMINATE: Tenant shall have the right to terminate this Lease with **respect to the Expansion Space only (the "Option to Terminate"), said** termination to be effective the last day of the sixty-sixth (66th) full calendar month after **the Expansion Rent Commencement Date (the "35 Termination Date"), provided:**

(a) Tenant is not then in default of any of the terms and conditions of this Lease beyond any applicable notice and cure period and this Lease is then in full force and effect;

(b) Landlord receives written notice from Tenant exercising this option not later than nine (9) months prior to the effective termination date; and

(c) Tenant delivers to Landlord, together with the above notice, a termination fee (the "Fee") in the amount of $323,758.00 which is equal to the then remaining unamortized balance of the following items: all brokers commissions paid by Landlord relative to this Twelfth Amendment to Lease; and the Landlord Allowance Landlord incurred relative to this Twelfth Amendment to Lease **(collectively, the "Costs"), such Costs to be amortized over the rental stream of this** Twelfth Amendment to Lease at 8% annual interest thereon.

In the event the entire Fee is not delivered to Landlord by Tenant together with the above Notice, Tenant's exercise of this option shall be null and void and of no force or effect. In the event that Tenant validly exercises this Option to Terminate with respect to the Expansion Space, then Tenant shall have no further obligation to pay rent for the Expansion Space following the 35 Termination Date.

6. OPTION TO RENEW: Provided that (i) this Lease is in full force and effect, (ii) Tenant is in possession of the Premises, and (iii) Tenant is not in default under any of the terms conditions and obligations of this Lease beyond any applicable notice and cure period, Tenant shall have the option to renew the term of this Lease with respect to the **Expansion Space for one additional period of five (5) years ("Option Period"). Said Option** Period shall commence on the day following the expiration date of the Amended Term. The tenancy resulting from the exercise of said option shall be on the same terms and conditions as set forth in this Lease, except that monthly Base Rent during the Option Period shall be as set forth below. Said Option Period may be exercised only upon written notice thereof which must be received by Landlord at least two hundred seventy (270) days prior to the expiration date of the Amended Term.

Monthly Base Rent for the Expansion Space during the Option Period shall be **recalculated and shall initially be the then "fair market rental value for the Premises" and** shall escalate four **percent (4%) per year. For the purposes hereof, the "fair market rental value of the Premises" shall be determined as follows: For a period of thirty (30) days**

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after Tenant's notice exercising its option to extend, Landlord and Tenant shall attempt to agree on the fair market rental value. If the parties are able to agree, the monthly Base Rent for the Expansion Space during the Option Period shall be such agreed upon fair market rental value. However, if Landlord and Tenant are unable to, or fail to agree upon such fair market rental value for the Option Period on or before such thirty (30) day period, the fair market rental value shall be determined by one (1) Rent Appraiser (as defined below) designated by Landlord and approved by Tenant, within ten (10) days following the expiration of such thirty (30) day period. If Landlord and Tenant so agree on a Rent Appraiser, such Rent Appraiser shall then make the determination of fair market rental value within thirty (30) days thereafter. If Landlord and Tenant do not agree on such Rent Appraiser selected by the Landlord, then Tenant shall select a Rent Appraiser within ten (10) days thereafter and the two Rent Appraisers shall determine the fair market rental value. If the determination by the two Rent Appraisers differs by less than ten (10%) percent, the arithmetic average of the two determinations shall be the fair market rental for the purpose of the above calculation. If the two determinations differ by more than ten (10%) percent, then the two Rent appraisers shall select a third Rent Appraiser who shall make the determination of the fair market value for the purpose of the above calculation. Rent Appraiser shall be an independent real estate appraiser or broker who shall have substantial professional experience in the appraisal and/or leasing of comparable space in the Chicago area and who shall be in all respects impartial and disinterested. Any and all fees charged by each Rent Appraiser shall be split equally between Landlord and Tenant.

If Tenant fails to exercise this option during the period when said option is available, or if this Lease is no longer in full force and effect for any reason, this option shall be void. Upon the expiration of the Option Period, Tenant shall have no further option to extend the Term of this Lease.

7. RIGHT OF FIRST OFFER: Tenant's Right of First Offer, as set forth in the Eighth Amendment to Lease, shall remain in full force and effect during the Amended Term and shall apply to the Expansion Space.

8. OCCUPANCY: The following is hereby added to the end of Section 3 of the Lease: "Tenant may operate during such days and hours as Tenant may determine, without the imposition of minimum or maximum hours of operation by Landlord, and Tenant shall have exclusive use of and full-time access to the Premises."

9. INSURANCE: The third paragraph of Section 10 is hereby amended by deleting the words ", which certificates shall state that such insurance coverage may not be changed or cancelled without at least thirty (30) days' prior notice to Landlord and Tenant."

10. REGULATORY COMPLIANCE: Landlord represents to Tenant that Landlord is not a "referring physician" or a "referral source" as to Tenant for services paid for by Medicare or a state healthcare program, as the terms are defined under any federal or state healthcare anti-referral or anti-kickback, regulation, interpretation, or opinion

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("Referral Source"). Each party represents that (1) it is not currently excluded from participation in any federal healthcare program, as defined under 42 U.S.C. Section 1320a-7b; (2) it is not currently excluded, debarred, suspended or otherwise ineligible to participate in federal procurement and non-procurement programs; and (3) it has not been convicted of a criminal offense that falls within the scope of 42 U.S.C. Section 1320a-7(a) but has not yet been excluded, debarred, suspended, or otherwise declared ineligible (each, an "Exclusion"), and agrees to notify the other party within 2 business days of learning of any such Exclusion or any basis therefor. If Landlord is or becomes a Referral Source and if this Lease is terminated for any reason before the first anniversary of the Expansion RCD, then Landlord and Tenant shall not enter into any similar agreement with each other for the Expansion Space before the first anniversary of the Expansion RCD.

The parties enter into the Lease with the intent of conducting their relationship in full compliance with applicable laws, regulations and guidelines, including, without limitation, the Anti-Kickback Statute and the Physician Self-Referral Statute, more commonly known as the Stark Law, pertaining to the use and occupation of the Premises (collectively, "Applicable Laws"). Each party represents that the entering into and performance of its obligations do not knowingly violate any Applicable Laws. Landlord shall notify Tenant of, and cooperate with, any request from a duly authorized government representative (e.g., Secretary of Health and Human Services, Comptroller General) for access to books, documents, and/or records related to this.

11. PROTECTED HEALTH INFORMATION: Landlord acknowledges and agrees that from time to time during the Term, Landlord and/or its employees, representatives, or assigns may be exposed to, or have access to, Protected Health Information ("PHI"), as defined by the Health Insurance Portability and Accountability Act of 1996 and related regulations ("HIPAA"), 45 CFR Parts 160 and 164. Landlord agrees that it will not use or disclose, and Landlord shall cause its employees and assigns not to use or disclose, PHI for any purpose unless in accordance with the requirements of HIPAA and all other applicable medical privacy laws. Landlord further agrees that, notwithstanding the rights granted to Landlord pursuant to this Lease, Tenant has the right to restrict access to the portions of the Premises where patient medical records are kept or stored or where such entry is prohibited by applicable healthcare laws, such areas to be deemed Secured Areas (as defined below), and Tenant may install locks at Tenant's expense on areas within the Premises as required for operation of its business, such as areas containing patient records or regulated narcotics and pharmaceuticals. Landlord further agrees that notwithstanding the rights granted to Landlord pursuant to this Lease, Tenant may designate certain portions of the Premises as "Secured Areas" if designation of such areas does not violate any applicable laws or prohibit Landlord free access to any fan room, mechanical room, or other portion of the Premises which is necessary to enter in connection with the repair, maintenance, operation, or upgrading of the Building systems and/or equipment or serving or providing services to other tenants in the Building, such as through riser closets or electrical rooms. Tenant shall not be required to furnish Landlord with door keys or other entry devices to the Secured Areas. Landlord agrees not to access or enter, nor allow its agents, representatives, employees, or

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independent contractors to access or enter Secured Areas, unless and until Tenant has been given 3 business days' prior written notice and then Landlord may only access the Secured Areas with an authorized representative of Tenant, which Tenant shall provide. If Landlord reasonably determines that it is necessary for Landlord to enter the Secured Areas in an emergency situation, Tenant must immediately permit such entry. In such event of an emergency, if Tenant is unavailable to provide such consent or if Tenant refuses to permit Landlord to enter into the Secured Areas, then Landlord may use such force as Landlord deems reasonably necessary to obtain entry into the Secured Areas and Landlord shall not be responsible for any damage to Tenant's property or the Premises caused by Landlord's forced entry.

12. BROKERS: Landlord and Tenant each represent and warrant to the other that the only brokers they have dealt with in connection with this Twelfth Amendment are Marc Realty LLC, and Mass Realty LLC, whose commissions and fees shall be paid by Landlord pursuant to a separate written agreement. Landlord and Tenant each agree to defend, indemnify and hold the other harmless from and against all claims by any other broker for fees, commissions or other compensation to the extent such broker alleges to have been retained by the indemnifying party in connection with the execution of this Twelfth Amendment. The provisions of this Paragraph shall survive the expiration or sooner termination of the Lease.

13. MISCELLANEOUS:

(a) All captions contained in this Twelfth Amendment are inserted only as a matter of convenience and in no way define, limit, or extend to scope or intent of this Twelfth Amendment or any provision hereof.

(b) This Twelfth Amendment shall be binding upon and inure to the benefit of the parties, their respective heirs, successors and assigns.

(c) This Twelfth Amendment sets forth the entire agreement between the parties and any prior writings or conversations are merged herein and extinguished. No amendment, alteration or other change of this Twelfth Amendment shall be enforceable unless set forth in a writing signed by the parties hereto.

(d) Except as otherwise provided herein, effective as of the Expansion Date, all duties and obligations of Tenant under the Lease relative to the Premises shall be duties and obligations of Tenant relative to the Total Space.

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IN WITNESS WHEREOF, the undersigned have executed this Twelfth Amendment as of the day and year first written above.

LANDLORD:

MARC REALTY LLC,
as Managing Agent aforesaid

By: DocuSigned by: Larry Weiner
Manager

TENANT:

SOLARIS HEALTH HOLDINGS, LLC,
a Delaware limited liability company

By: Signed by:
Name: Dr. Richard Harris
Its: Market president

ACKNOWLEDGED AND AGREED FOR PURPOSES OF CONFIRMING THE CONTINUING LIABILITY OF SUBTENANT UNDER THE LEASE:

SUBTENANT:

UROPARTNERS, LLC,
an Illinois limited liability company

By: DocuSigned by: Richard Wooten
Name: Richard Wooten
Its: COO

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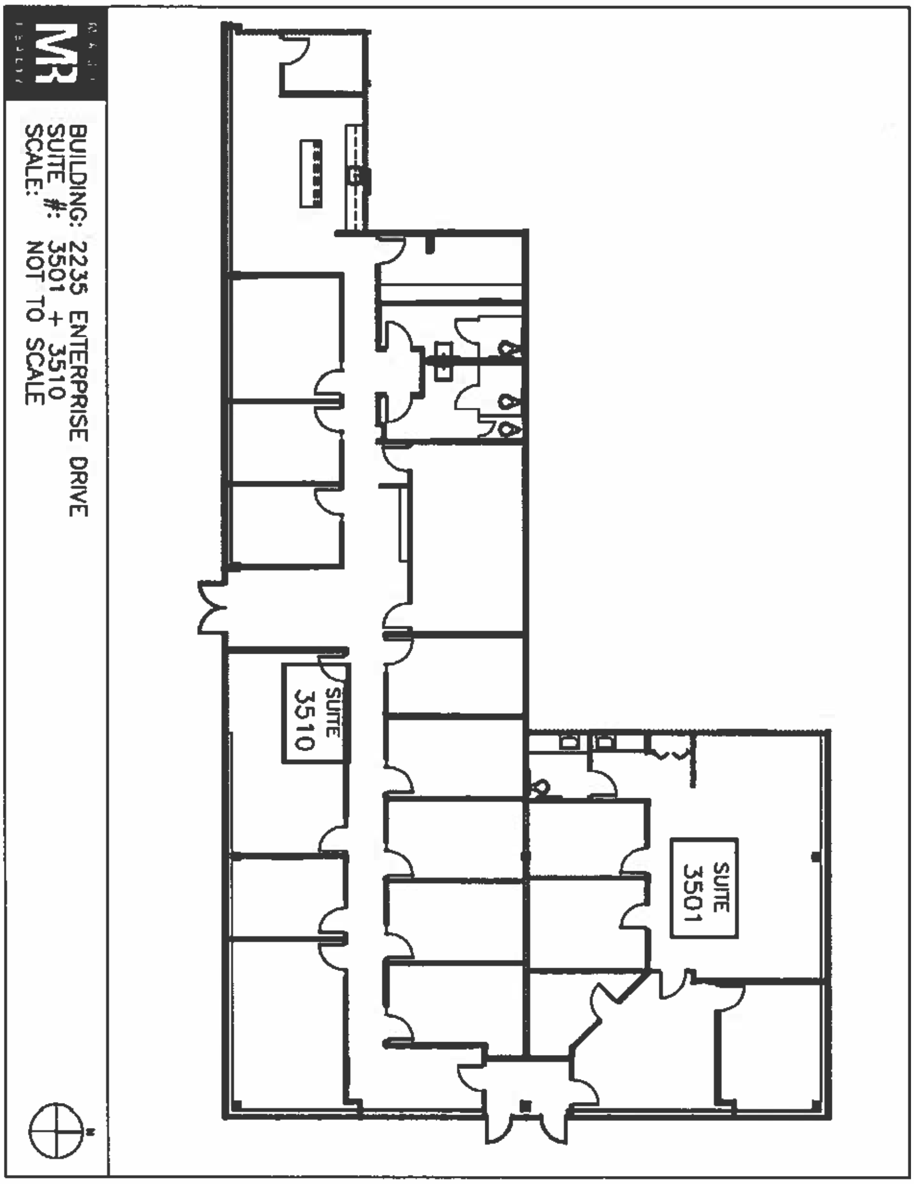
EXHIBIT A



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UroPartners, LLC
2245 Enterprise Drive
Suite 4506
Westchester, Illinois 60154

November 30, 2022

Enterprise Centre LLC
c/o Marc Realty LLC
55 East Jackson Boulevard
Suite 500
Chicago, Illinois 60604

Re: Consent to Assignment of Lease

Dear Sir or Madam:

We are pleased to announce that UroPartners, LLC ("Tenant") and Solaris Health Holdings, LLC and its affiliates ("Solaris") plan to enter into an agreement that would result in the assignment of certain assets, including the Agreement (as defined below), of Tenant to Solaris (the "Proposed Transaction").

Tenant and Enterprise Centre LLC ("Landlord") are parties to that certain Office Building Lease for the premises located at 2225 Enterprise Drive, Suite 2511, Westchester, Illinois 60154 (the "Agreement"), dated August 15, 2005 as subsequently amended. Tenant hereby requests that Landlord consent to the assignment of the Agreement to Solaris in connection with the Proposed Transaction, waive any breach or default rights, including any rights of termination, that it has under the Agreement as the result of the Proposed Transaction, and further consent to a sublease of the premises leased under the Agreement from Solaris to Tenant or otherwise allow the occupancy or use of all or any portion of the premises leased under the Agreement by Tenant (collectively, the "Sublease"). Tenant shall remain fully liable throughout the entire term of the Agreement for the performance and observance of all terms, covenants, and conditions contained in the Agreement.

By signing this letter agreement, Landlord (i) consents to the assignment of the Agreement to Solaris in connection with the Proposed Transaction, (ii) acknowledges and agrees that the Agreement will continue in full force and effect and shall continue to be in full force and effect following the Proposed Transaction, (iii) consents to the Sublease, which shall be on all of the same terms and conditions of the Agreement, (iv) waives any right of recapture, breach or default of the Agreement or any right to terminate the Agreement as a result of the Proposed Transaction or other remedies Landlord may be entitled to under the Agreement in connection with the assignment and the Sublease, and (v) acknowledges and agrees that neither the assignment nor the Sublease shall eliminate or adversely affect Solaris's option rights as the tenant, if any, set forth in the Agreement. In the event, however, that the Proposed Transaction is not consummated, this consent shall be of no force and effect. We will notify you if the Proposed Transaction is not completed.

This letter may be executed in any number of counterparts and by different parties on separate counterparts. Delivery of an executed counterpart of this letter by email transmission of a .pdf (or similar) file format document shall be as effective as delivery of a manually executed counterpart of this letter.

Please confirm Landlord's consent and agreement to all of the foregoing by executing this letter in the space below and returning the same to Morgan T. D'Arcy via email at mdarcy@pfs-law.com as soon as possible.

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If you have any questions or concerns regarding the foregoing, please contact Morgan T. D'Arcy at your convenience.

Thank you in advance for your prompt attention to this request.

Yours truly,

UroPartners, LLC

By:_____
Name: Richard Harris
Title: Manager

The undersigned hereby acknowledges and agrees to the terms of this letter agreement without modification of the Agreement. It being understood that nothing contained herein or in the Proposed Transaction shall release or discharge Tenant from its liabilities and obligations under the Agreement or constitute a waiver by the undersigned of the continuing obligation of Tenant under the Agreement to secure the prior written consent of the undersigned to any further assignment of the Lease.

Enterprise Centre LLC,

By:_____
Name: Laurence Weiner
Title: Manager

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Thank you in advance for your prompt attention to this request.

Yours truly,

UroPartners, LLC

By:_____
Name: Richard Harris
Title: Manager

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OFFICE BUILDING LEASE

ENTERPRISE Center
2205 – 2255 Enterprise Drive
Westchester, Illinois 60154
Between

MARC REALTY LLC

as Managing Agent for Landlord

and

UROPARTNERS, LLC

as Tenant

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OFFICE BUILDING LEASE

THIS LEASE is made as of the 15th day of August, 2005, by and between **MARC REALTY LLC**, as Managing Agent for Beneficiaries of North Star Trust Company Title Holding Land Trust, ("Landlord"), and **UROPARTNERS, LLC**, an Illinois limited liability company, ("Tenant").

Landlord hereby leases to Tenant and Tenant hereby accepts the premises designated on the plan attached hereto as Exhibit "A", commonly described as Suite 2511 (being approximately 2,062 rentable square feet) (the "Premises") in the building located on the Land (the "Land") commonly known as Enterprise Center, 2205 – 2255 Enterprise Drive (the "Complex"), located at 2225 Enterprise Drive, Westchester, Illinois 60154, (the "Building") for the term of five (5) years commencing on the 1st day of December, 2005 and terminating on the 30th day of November, 2010 (the "Term"), both dates inclusive, unless sooner terminated as provided herein.

In consideration thereof, Landlord and Tenant covenant and agree as follows:

1. **BASE RENT**. Tenant shall pay to Landlord at the office of Landlord or at such other place as Landlord may designate the monthly Base Rent as follows:

PERIOD	MONTHLY BASE RENT
December 1, 2005 through November 30, 2006	$2,835.00
December 1, 2006 through November 30, 2007	$2,977.00
December 1, 2007 through November 30, 2008	$3,126.00
December 1, 2008 through November 30, 2009	$3,282.00
December 1, 2009 through November 30, 2010	$3,446.00

Each monthly Base Rent payment shall be made in advance on the first day of each and every month during the Term, without any set-off or deduction whatsoever, except that Tenant shall pay the first full month's installment at the time of execution of this Lease. If the Term commences other than on the first day of a month or ends other than on the last day of the month, the Base Rent for such month shall be prorated, and the prorated rent for the portion of the month in which the Term commences shall also be paid at the time of execution of this Lease.

2. **ADDITIONAL RENT**. All amounts required or provided to be paid by Tenant under this Lease in addition to Base Rent shall be deemed rent, and the failure to pay the same shall be treated in all events as the failure to pay rent.

3. **OCCUPANCY**. Tenant shall use and occupy the Premises for medical laboratory and general office purposes and no other purpose.

4. **CONDITION OF PREMISES**. The Tenant's taking possession shall be conclusive evidence that the Premises and the Building were in good order and satisfactory condition when the Tenant took possession, and Tenant, having examined the Premises, accepts same in "AS-IS" condition. No promise of the Landlord to alter, remodel or improve the Premises or the Building and no representation respecting the condition of the Premises or the Building have been made by the Landlord to the Tenant other than as are contained in the Workletter attached hereto.

5. **POSSESSION**. In the event the Premises shall not be completed and ready for occupancy on the date fixed for the commencement of the Term or in the event Landlord is unable to deliver possession on such date by reason of the holding over or retention of possession by any tenant or occupant, this Lease shall nevertheless continue in force and effect but Rent (including Additional Rent) shall abate until the Premises are ready for occupancy or until the Landlord is able to deliver possession, as the case may be, and Landlord shall have no other liability whatsoever on account thereof; provided, however, there shall be no abatement of Rent if the Premises are not ready for occupancy because of the failure to complete the installation of special equipment, fixtures or materials ordered by Tenant, or because of any delays resulting from Tenant's failure to approve or submit plans and specifications timely in accordance with the Workletter attached hereto or other written agreement or resulting from changes or additions to Tenant's plans and specifications after the initial submission hereof. The Premises shall not be deemed incomplete or not ready for occupancy if only insubstantial details of construction, decoration or mechanical adjustments remain to be done. Except as otherwise agreed upon in writing, the determination of Landlord's architect shall be final and conclusive on both Landlord and Tenant as to whether the Premises are completed and ready for occupancy. If Tenant shall take possession of any part of the Premises prior to the date fixed above as the first day of the Term (which Tenant may not do without Landlord's prior written consent), all of the covenants and conditions of this Lease shall be binding upon the parties hereto with respect to such part of the Premises as if the first day of the Term has been fixed as the date when Tenant entered such possession and Tenant shall pay to Landlord rent for the period of such occupancy prior to the first day of the Term of this Lease at the rate of the annual Base Rent set forth in Paragraph 1 hereof for the portion of the Premises so occupied. Under no circumstances shall the occurrence of any of the events hereinabove referred to be deemed to accelerate or defer the stated expiration date of the Term.

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In the event Landlord fails to substantially complete the Work as set forth in the Workletter, through no fault of Tenant, within ninety (90) days after the Commencement of the Term, Tenant shall have the right to cancel this Lease by written notice to Landlord.

6. A. <u>SERVICES</u>. Landlord shall provide the following services on all days during the Term excepting Sundays and holidays, unless otherwise stated. (Holidays being New Year's Day, Memorial Day, July 4th, Labor Day, Thanksgiving Day and Christmas Day):

(a) Rooftop condensing unit(s), air handler(s) and heating unit(s) for Tenant's use, including routine inspections thereof.

(b) Electricity for all standard receptacles and lighting fixtures and also for Tenant's heating (if electric heating), cooling, and for all air conditioning units, and incidental uses, and gas for Tenant's heating (if gas heat) which electricity and gas shall be separately metered and billed directly to, and be the sole responsibility of, Tenant by the utility company furnishing such service. Tenant shall bear the cost of maintenance of lighting fixtures and replacement of ballasts and lamps. The electricity for Tenant's incidental uses shall be limited to that used for equipment and accessories normal to office usage, and shall include electricity for photocopy machines, electronic data processing equipment, and computers, but shall exclude special heating, cooling and humidification equipment and other out of the ordinary electric equipment. If Tenant requires electricity for equipment and accessories not normal to office usage, Tenant shall procure electricity for such equipment and accessories, at Tenant's expense, from the local public utility company servicing the Building. Tenant shall pay for the cost of installing any additional required meters.

(c) Janitor services Monday through Friday in and about the Premises.

(d) City water from the regular Building outlets for drinking, lavatory and toilet purposes.

(e) Snow removal service for walks within a reasonable time after a snowfall.

(f) Outside and inside window washing about the Premises at intervals to be determined by Landlord.

Tenant agrees that Landlord shall not be liable in damages, by abatement of rent or otherwise, for failure to furnish or delay in furnishing any service when such failure or delay is occasioned, in whole or in part, by repairs, renewals or improvements, by any strike, lockout or other labor trouble, by inability to secure electricity, gas, water or other fuel at the Building after reasonable effort so to do, by any accident or casualty whatsoever, by the act or default of Tenant or other third parties, or by any cause beyond the reasonable control of Landlord, and such failures or delays shall never be deemed to constitute an eviction or disturbance of the Tenant's use and possession of the Premises or relieve the Tenant from paying rent or performing any of its obligations under this Lease.

All charges for services for which Tenant is required to pay hereunder shall be due and payable at the same time as the installment of rent with which they are billed, or, if billed separately, shall be due and payable within ten (10) days after such billing. If Tenant shall fail to make payment for any such services, Landlord may, without notice to Tenant, discontinue any or all of such services and such discontinuance shall not be deemed to constitute an eviction or a disturbance of the Tenant's use and possession of the Premises or relieve Tenant from paying rent or performing any of its other obligations under this Lease.

B. <u>UTILITY DEREGULATION</u>:

(a) <u>Landlord Controls Selection</u>. Commonwealth Edison ("Electric Service Provider") is the utility company currently providing electricity service for the Building. Notwithstanding the foregoing, if permitted by law, Landlord shall have the right, at Landlord's sole option, at any time and from time to time during the Term to either contract for electric service from a new or different company or companies providing electric service (each such company shall hereinafter be referred to as an "Alternate Service Provider") or continue to either contract for service from the Electric Service Provider.

(b) <u>Tenant Shall Give Landlord Access</u>. Tenant shall cooperate with Landlord, the Electric Service Provider, and any Alternate Service Provider at all times and, as reasonably necessary, shall allow Landlord, Electric Service Provider, and any Alternate Service Provider reasonable access to the Building's water lines, electric lines, feeders, risers, wiring, and any other machinery or service apparatus within the Premises.

(c) <u>Landlord Not Responsible for Interruption of Service</u>. Landlord shall in no way be liable or responsible for any loss, damage, or expense that Tenant may sustain or incur by reason of any change, failure, interference, disruption, defect, interruption or delay in the supply or character of the electric energy furnished to the Premises or the Building, or if the quantity or character of the electric energy supplied by the electric Service Provider or any Alternate Service Provider is no longer available or suitable for Tenant's requirements, and no such change, failure, defect, unavailability, or

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unsuitability shall constitute an actual or constructive eviction, in whole or in part, or entitle Tenant to any abatement or diminution of rent, or relieve Tenant from any of its obligations under the Lease.

C. RENT ABATEMENT. Notwithstanding anything to the contrary contained herein, if, as a result of the negligence of Landlord, its agents or employees, there is an interruption or discontinuance in the furnishing by Landlord of any of the aforementioned services to the Premises which results in Tenant being unable to operate at the Premises, and Tenant is closed at the Premises, for a period in excess of five (5) consecutive days after notice to Landlord by Tenant, the monthly Base Rent required under this Lease shall abate from the end of such period until the earlier of the date Tenant reopens at the Premises or such time as the service is restored such that Tenant is again reasonably able to operate at the Premises. In the event that such interruption or discontinuance which is within Landlord's reasonable control, and which is not being diligently remedied by Landlord, results in Tenant being unable to operate at the Premises, and Tenant is closed at the Premises, for a period in excess of sixty (60) consecutive days after notice to Landlord by Tenant, then Tenant shall have the right to terminate this Lease by written notice to Landlord.

7. REPAIRS. Tenant will at Tenant's own expense, keep the Premises in good order, repair and condition during the Term, and Tenant shall promptly and adequately repair all damage to the Premises and replace or repair all damaged or broken plumbing, fixtures and appurtenances with plumbing, fixtures or appurtenances of substantially the same grade, make and quality, under the supervision and subject to the approval of the Landlord, and within any reasonable period of time specified by the Landlord. Tenant's obligation for repairs shall not include any obligation to make structural repairs, including the walls, roof, floors and internal pipes, conduits, ducts, lines, wires, drains and flues and all other facilities for plumbing, electricity, or heating and air conditioning units, unless such repairs or replacement are caused by the negligence of Tenant. If the Tenant does not make its required repairs and replacements, Landlord may, but need not, do so, and Tenant shall pay Landlord the cost thereof forthwith upon being billed for same.

Landlord may, but shall not be required to, enter the Premises at all reasonable times to make such repairs, alterations, improvements and additions, including, without limitation, conduits, ducts, internal pipes, lines, wires, drains and flues and all other facilities for plumbing, electricity, heating and air conditioning, as Landlord shall desire or deem necessary to the Premises or to the Building or to any equipment located in the Building or as Landlord may be required to do by government authority or court order or decree.

8. ADDITIONS AND ALTERATIONS. Tenant shall not, without the prior written consent of Landlord, make any alterations, improvements or additions to the Premises. Landlord need not give any such consent but if Landlord does, it may impose such conditions with respect thereto as Landlord deems appropriate, including, without limitations, requiring Tenant to furnish Landlord with security for the payment of all costs to be incurred in connection with such work and insurance against liabilities which may arise out of such work, as determined by Landlord. The work necessary to make any alterations, improvements or additions to the Premises shall be done at Tenant's sole cost by contractors. Tenant shall promptly pay to Landlord or to Tenant's contractors, as the case may be, when due, the cost of all such work and of all decorating required by reason thereof, and upon completion deliver to Landlord, if payment is made directly to contractors, evidence of payment, contractors' affidavits and full and final waivers of all liens for labor, services or materials, and Tenant shall defend and hold Landlord and the Land and Building harmless from all costs, damages, liens and expenses related thereto.

All work done by Tenant or its contractors pursuant to this Paragraph 8 or pursuant to Paragraph 7 hereof shall be done in first-class workmanlike manner using only good grades of materials and shall comply with all insurance requirements and all applicable laws and ordinances and rules and regulations of governmental departments or agencies. All required permits shall be obtained by Tenant at Tenant's expense.

If Tenant desires signal communications, alarm or other utility or service connection installed or changed, the same shall be made at the expense of Tenant, with prior written consent and under direction of Landlord and subject to the conditions of the first paragraph of this Paragraph 8 hereof.

All alterations, improvements and additions to the Premises, permanent in character, made or paid for by Landlord or Tenant, shall without compensation to Tenant become Landlord's property at the termination of this Lease by lapse of time or otherwise and shall, unless Landlord requests their removal (in which case Tenant shall remove the same as provided in Paragraph 16), be relinquished to Landlord in good condition, ordinary wear excepted.

Tenant shall not affix or install any wall treatments or wall coverings, of any type or nature (other than paint), within the Premises, without Landlord's prior written consent.

9. COVENANT AGAINST LIENS. Tenant has no authority or power to cause or permit any lien or encumbrance of any kind whatsoever whether created by act of Tenant, operation of law or otherwise, to attach to or be placed upon Landlord's title or interest in the Land, Building or Premises, and any and all liens and encumbrances created by Tenant shall attach to Tenant's interest only. Tenant covenants and agrees not to suffer or permit any lien of mechanics or materialmen or others to be placed against the Land, Building or the Premises with respect to work or services claimed to have been performed for or materials claimed to have been furnished to Tenant or the Premises, and in case of any such lien attaching, Tenant covenants

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and agrees immediately to cause it to be released and removed of record or bonded in manner satisfactory to Landlord.

10. **INSURANCE**. Landlord and Tenant each agrees to have all fire and extended coverage and other property damage insurance which it carries with respect to the Building or Premises or to the property located in the Premises endorsed with a clause which reads substantially as follows: "This insurance shall not be invalidated should the insured waive in writing prior to a loss any or all rights of recovery against any party for loss occurring to the property described herein." Landlord and Tenant each hereby waives all claims for recovery from the other for any loss or damage to the Building or Premises or to the contracts thereof which is insured under valid and collectible insurance policies, subject to the condition that this waiver shall be effective only when the waiver is either permitted by such insurance policy or when, by the use of good faith efforts, such waiver could have been included in the applicable insurance policy at no additional expense.

Tenant shall carry the following insurance in companies satisfactory to Landlord:

(a) Comprehensive general liability insurance during the entire term hereof covering both Tenant and Landlord as insureds with terms and in companies satisfactory to Landlord with limits of not less than One Million ($1,000,000) Dollars combined single limit per occurrence for Personal Injury, Death and Property Damage or in such other amounts as Landlord shall reasonably require.

(b) Insurance against all risks (including sprinkler leakage, if applicable), for the full replacement cost of all additions, improvements and alterations to the Premises (except to the extent the same are included within the definition of "Work", but not "Additional Work", in the Workletter attached hereto), and of all office furniture, trade fixtures, office equipment, merchandise and all other items of Tenant's property on the Premises.

Tenant shall, prior to the commencement of the Term (or within ten (10) days after written notice from Landlord to Tenant in the case of additional coverage or increased amounts of coverage), furnish to Landlord certificates evidencing such coverage, which certificates shall state that such insurance coverage may not be changed or cancelled without at least thirty (30) days' prior written notice to Landlord and Tenant.

Tenant shall comply with all applicable laws and ordinances (including, but not limited to environmental laws), all orders and decrees of court and all requirements of other governmental authority, and shall not directly or indirectly make any use of the Premises, or use, store or dispose of within the Premises or the Building materials, which may thereby be prohibited or not be approved by any appropriate governmental agency or be dangerous to person or property or which may jeopardize any insurance coverage, or may increase the cost of insurance or require additional insurance coverage.

If Tenant does not take out the insurance required pursuant to this Paragraph 10 or keep the same in full force and effect, Landlord may, but shall not be obligated to take out the necessary insurance and pay the premium therefore, and Tenant shall repay to Landlord, as Additional Rent, the amount so paid promptly upon demand. In addition, Landlord may recover from Tenant and Tenant agrees to pay, as Additional Rent, any and all reasonable expenses (including attorneys' fees) and damages which Landlord may sustain by reason of the failure to Tenant to obtain and maintain such insurance, it being expressly declared that the expenses and damages of Landlord shall not be limited to the amount of the premiums thereon.

In no event shall Tenant permit in the Premises flammables such as gasoline, turpentine, kerosene, naphtha and benzene, or explosives or any other article of intrinsically dangerous nature, and in no event shall Tenant, its agents, employees or invitees bring any such flammables or other articles into the Building. If by reason of the failure of Tenant to comply with the provisions of this paragraph, any insurance coverage is jeopardized or insurance premiums are increased, Landlord shall have the option either to terminate this Lease or to require Tenant to make immediate payment of the increased insurance premium.

Tenant shall not bring, keep discharge or release or permit to be brought, kept discharged or released, in or from the Premises of the Building any toxic or hazardous substance, material or waste or any other contaminant or pollutant other than (i) non-reportable quantities of such substances when found in commonly used household cleansers, office supplies and general office equipment and (ii) reasonable quantities of lab chemicals and other substances normally used in Tenant's business operations (collectively, "Hazardous Materials"), and any Hazardous Materials shall be used, kept, stored and disposed of in strict accordance with all applicable federal, state and local laws. Tenant shall comply with all applicable federal, state and local laws. Tenant shall comply with all applicable federal, state and local reporting and disclosure requirements, with respect to Hazardous Materials, applicable to its business operations in the Premises. Upon the written request of Landlord, Tenant shall provide periodic written reports of the type and quantities of any and all types of substances, materials, waste and contaminants (whether or not believed by Tenant to be Hazardous Materials) used, stored or being disposed of by Tenant in or from the Premises. If Landlord in good faith determines that any of such substances create a risk to the health and safety of Tenant's employees and invitees or to any other tenant or invitee of the Building, Tenant shall, upon demand by Landlord, take such remedial action, at the sole cost and expense of Tenant (including, without limitation, removal in a safe and lawful manner of any Hazardous Materials from the Premises), as Landlord deems necessary or advisable or as is required by applicable law.

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11. **FIRE OR CASUALTY**. If the Premises or the Building (including machinery or equipment used in its operation) shall be damaged by fire or other casualty and if such damage does not render all or a substantial portion of the Premises untenantable, then Landlord shall repair and restore the same with reasonable promptness. If any such damage renders all or a substantial portion of the Premises or of the Building, untenantable, Landlord shall with reasonable promptness after the occurrence of such damage estimate the length of time that will be required to substantially complete the repair and restoration of such damage and shall by notice advise Tenant of such estimate. If such estimate is that the amount of time required to substantially complete such repair and restoration will exceed one hundred eighty (180) days from the date such damage occurred, then either Landlord or Tenant (but as to Tenant, only if all or a substantial portion of the Premises are rendered untenantable) shall have the right to terminate this Lease as of the date of such damage upon giving notice to the other at any time within twenty (20) days after Landlord gives Tenant the notice containing said estimate (it being understood that Landlord may, if it elects to do so, also give such notice of termination together with the notice containing such estimate). Unless this Lease is terminated as provided in the preceding sentence, Landlord shall proceed with reasonable promptness to repair and restore the Premises, subject to reasonable delays for insurance adjustments and delays caused by matters beyond Landlord's reasonable control, and also subject to zoning laws and building codes then in effect. Notwithstanding anything to the contrary herein set forth (a) Landlord shall have no liability to Tenant, and Tenant shall not be entitled to terminate this Lease, in the event such repairs and restoration are not in fact completed within the time period estimated by Landlord, as aforesaid, or within said one hundred eighty (180) days; and (b) Tenant shall not have the right to terminate this Lease pursuant to this Section if the damage or destruction was caused by the act or neglect of Tenant, its agents or employees.

Notwithstanding anything to the contrary herein set forth, Landlord shall have no duty pursuant to this Paragraph 11 to repair or restore any portion of the alterations, additions or improvements in the Premises or the decoration thereto except to the extent that such alterations, additions, improvements and decoration are included within the definition of "Work" (but not "Additional Work") in the Workletter attached hereto or otherwise agreed upon in writing by the parties. If Tenant wants any other or additional repairs or restoration and if Landlord consents thereto, the same shall be done at Tenant's expense subject to all the provisions of Paragraph 8 hereof.

In the event any such damage not caused by the act or neglect of Tenant, its agents or servants, renders the Premises untenantable and if this Lease shall not be cancelled and terminated by reason of such damage, then the rent (including Base Rent and Additional Rent) shall abate during the period beginning with the date of such damage and ending with the date when the Premises are again rendered tenantable. Such abatement shall be in an amount bearing the same ratio of the total amount of rent for such period as the untenantable portion of the Premises from time to time bears to the entire Premises.

12. **WAIVERS OF CLAIMS - INDEMNIFICATION**. Tenant agrees that, to the extent not prohibited by law, Landlord and its officers, agents, servants and employees shall not be liable for any damage either to person or property or resulting from the loss or use thereof sustained by Tenant or by other persons due to the Building or any part thereof or any appurtenances thereof becoming out or repair, or due to the happening of any accident or event in or about the Building, or due to any act or neglect of any tenant or occupant of the Building or of any other person. This provision shall apply particularly (but not exclusively) to damage caused by gas, electricity, snow, frost, steam, sewage, sewer gas or odors, fire, water or by the bursting or leaking of pipes, faucets, sprinklers and plumbing fixtures, and shall apply without distinction as to the person whose act or neglect was responsible for the damage and whether the damage was due to any of the causes specifically enumerated above or to some other cause of an entirely different kind. Tenant further agrees that all personal property upon the Premises, or upon loading docks, receiving and holding areas, or any freight elevators of the Building, shall be at the risk of Tenant only, and that Landlord shall not be liable for any loss or damage thereto or theft thereof.

Without limitation of any other provisions hereof, Tenant agrees to defend, protect, indemnify and save harmless Landlord of and from all liability to third parties arising out of the acts of Tenant and its servants, agents, employees, contractors, suppliers and workmen or invitees.

13. **NONWAIVER**. No waiver of any provision of this Lease shall be implied by any failure of Landlord to enforce any remedy on account of the violation of such provision even if such violation be continued or repeated subsequently, and no express waiver shall affect any provision other than the one specified in such waiver and that one only for the time and in the manner specifically stated. Subject to the rights of Landlord in Paragraph 17, no receipt of monies by Landlord from Tenant after the termination of this Lease will in any way alter the length of the Term or of Tenant's right to possession hereunder or after the giving of any notice shall reinstate, continue or extend the Term or affect any notice given Tenant prior to the receipt of such monies, it being agreed that after the service of notice or the commencement of a suit or after final judgment for possession of the Premises, Landlord may receive and collect any rent due, and the payment of said rent shall not waive or affect said notice, suit or judgment.

14. **CONDEMNATION**. If the whole or any part of the Building shall be taken or condemned for any public or quasi-public use or purpose, the Term, at the option of Landlord, shall end upon the date when the possession of the part so taken shall be required for such use or purpose and Landlord shall be entitled to receive the entire award without any payment to Tenant. Rent shall be apportioned as of the date of such termination.

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15. **ASSIGNMENT AND SUBLETTING**. Tenant shall not, without the prior written consent of Landlord (i) assign this Lease or any interest hereunder; (ii) permit any assignment of this Lease by operation of law; (iii) sublet the Premises or any part thereof; (iv) permit the use of the Premises by any parties other than Tenant, its agents and employees. In no event shall this Lease be assigned or assignable by voluntary or involuntary bankruptcy proceedings or otherwise, and in no event shall this Lease or any rights or privileges hereunder be an asset of Tenant under any bankruptcy, insolvency or reorganization proceedings. Tenant shall give Landlord written notice of any proposed assignment or subleasing, which notice shall contain the proposed principal terms thereof, and upon receipt of such notice, Landlord shall have the option to cancel the Lease in the case of a proposed assignment or a proposed subleasing of all of the Premises, or if Tenant proposes to sublease less than all of the Premises, to cancel the Lease with respect to the portion to be subleased, in which latter event the Base Rent and Additional Rent shall be adjusted on a prorata square foot of rentable area basis. The foregoing option to cancel shall not apply in the case of a proposed sublease of all or a portion of the Premises to an affiliate corporation under the same control (as hereinafter defined) as Tenant. If Landlord wishes to exercise such option to cancel, Landlord shall, within fifteen (15) days after Landlord's receipt of such notice from Tenant, send to Tenant a notice so stating and in such notice Landlord shall specify the date as of which such cancellation is effective, which date shall be not less than thirty (30) and not more than ninety (90) days after the date on which Landlord sends such notice. If Landlord does not elect to cancel, as aforesaid, or if Landlord does not have an option to cancel, Landlord agrees not to unreasonably withhold its consent to any proposed assignment or subletting if the proposed assignee or sublessee (in Landlord's judgment) has a financial condition comparable to or better than that of Tenant, has a good reputation in the business community and agrees to use the Premises for purposes satisfactory to Landlord. Further, in the event of a proposed subletting, Tenant and the proposed sublessee shall use Landlord's form sublease agreement unless otherwise agreed by Landlord. No assignment of this Lease shall be effective unless the assignee shall execute an appropriate instrument assuming all of the obligations of Tenant hereunder and unless Tenant acknowledges therein its continued liability under this Lease. In addition, Tenant shall pay to Landlord any attorney's fees and expenses incurred by Landlord in connection with any proposed assignment or subleasing, whether or not Landlord consents to such assignment or subleasing.

Notwithstanding anything to the contrary in this Section, if Tenant at any time during the Term of this Lease is a closely-held corporation and if during the Term of this Lease, the ownership of the shares of stock which constitute control of Tenant changes other than by reason of gift or death, Tenant shall notify Landlord of such change within five (5) days thereof, and Landlord at its option may at any time thereafter terminate this Lease by giving Tenant at least sixty (60) days prior written notice of said termination. The term "control" as used herein means the power to directly or indirectly direct or cause the direction of, the management or policies of the Tenant. A change or series of changes in ownership of stock which would result in direct or indirect change in ownership by the stockholders of an affiliated group of shareholders of less than fifty percent (50%) of the stock outstanding as of the date of execution of this Lease by Tenant shall not be considered a change of control.

16. **SURRENDER OF POSSESSION**. Upon the expiration of the Term or upon the termination of Tenant's right of possession, whether by lapse of time or at the option of Landlord as herein provided, Tenant shall at once surrender the Premises to Landlord in good order, repair and condition, ordinary wear excepted, and remove all of its property therefrom, and if such possession is not immediately surrendered Landlord may forthwith re-enter the Premises and repossess itself thereof and remove all persons and effects therefrom, using such force as may be necessary, without being deemed guilty of any manner of trespass, eviction or forcible entry or detainer and without thereby relinquishing any right given to Landlord hereunder or by the operation of law. Without limiting the generality of the foregoing, Tenant agrees to remove at the termination of the Term or of its right of possession the following items of property: office furniture, trade fixtures, office equipment, merchandise and all other items of Tenant's property on the Premises, and such (but only such) alterations, improvements and additions as may be requested by Landlord, and Tenant shall pay to Landlord upon demand the cost of repairing any damage caused by any such removal. If Tenant shall fail or refuse to remove any such property from the Premises, Tenant shall be conclusively presumed to have abandoned same, and title thereof shall thereupon pass to Landlord without any cost either by set-off, credit, allowance or otherwise, and Landlord may at its option accept the title to such property or at Tenant's expense may (i) remove the same or any part in any manner that Landlord shall choose, and (ii) store, destroy or otherwise dispose of the same without incurring liability to Tenant or any other person.

17. **HOLDING OVER**. Tenant shall pay to Landlord one hundred fifty percent (150%) of the Base Rent set forth in Paragraph 1 hereof and any appropriate Additional Rent then applicable (the "Holdover Rate") for each month or portion thereof for which Tenant shall retain possession of the Premises or any part thereof after the termination of the Term or Tenant's right of possession, whether by lapse of time or otherwise, and also shall pay all damages sustained by Landlord on account thereof. The provisions of this paragraph shall not be deemed to limit any rights of Landlord. At the option of Landlord, expressed in a written notice to Tenant and not otherwise, such holding over shall constitute either (i) a month-to-month tenancy upon the then applicable terms and conditions set forth herein, or (ii) a tenancy at sufferance, or (iii) a renewal of this Lease for a period of one (1) year at the Base Rent and Additional Rent as would be applicable for such year. If no such notice is served, then a tenancy at sufferance shall be deemed created at the Holdover Rate.

18. **ESTOPPEL CERTIFICATE**. The Tenant agrees from time to time upon not less than ten (10) days prior request by Landlord or by any Lender which is the holder of a lien against the Land or Building

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("Lender"), the Tenant or Tenant's duly authorized representative having knowledge of the following facts, will deliver to Landlord a statement in writing certifying (i) that this Lease is unmodified and in full force and effect (or if there have been modifications that the Lease as modified is in full force and effect); (ii) the dates to which the rent and other charges have been paid; (iii) that the Landlord is not in default under any provision of this Lease, or, if any default, the nature thereof in detail, and (iv) to such other matters pertaining to this Lease as Landlord reasonably requires. If Tenant fails to deliver such statement within the ten (10) day period referred to above, Tenant does hereby make, constitute and irrevocably appoint Landlord as its attorney-in-fact coupled with an interest and in its name, place and stead so to do.

19. <u>SUBORDINATION</u>. Tenant hereby agrees that this Lease shall automatically be subject and subordinate to (i) any indenture of mortgage or deed of trust that may hereafter be placed upon the Building and to all renewals, replacements and extensions thereof, and to all amounts secured thereby, except to the extent that any such indenture of mortgage or deed of trust provides otherwise, and (ii) any ground or underlying lease. Tenant shall at Landlord's request execute such further instruments or assurances as Landlord may reasonably deem necessary to evidence the subordination of this Lease to the lien of any such indenture or mortgage or deed of trust or to any such ground or underlying lease or to acknowledge that this Lease is superior to such lien, as the case may be.

Should any prospective mortgage or ground lessor require any modification of this Lease, which modification(s) will not cause an increased cost or expense to Tenant or in any other way materially and adversely change the rights and obligations of Tenant hereunder, then and in such event, Tenant agrees that this Lease may be so modified and agrees to promptly execute and deliver whatever documents are required therefor.

Tenant shall, in the event of a sale or assignment of Landlord's interest in the Land, the Building, or this Lease, or if the Land or the Building comes into the hands of a Lender, ground lessor or any other person whether because of a mortgage foreclosure, exercise of a power of sale under a mortgage, deed-in-lieu of foreclosure, termination of the ground lease, or otherwise, attorn to the purchaser or such Lender or other person and recognize the same as Landlord hereunder. Tenant shall execute, at the request of Landlord, such purchaser, Lender, or such other person entitled to the attornment by Tenant under this paragraph, any attornment agreement required by such person to be executed, and containing such provisions as such mortgagee, ground lessor or other person requires.

20. <u>CERTAIN RIGHTS RESERVED BY LANDLORD</u>. Landlord shall have the following rights, each of which Landlord may exercise without notice to Tenant and without liability to Tenant for damage or injury to property, person or business on account of the exercise thereof, and the exercise of any such rights shall not be deemed to constitute an eviction or disturbance of Tenant's use or possession of the Premises and shall not give rise to any claim for set-off or abatement of rent or any other claim:

(a) To change the street address upon no less than one hundred twenty (120) day notice.

(b) To install, affix and maintain any and all signs on the exterior and on the interior of the Building.

(c) To decorate or to make repairs, alterations, additions or improvements, whether structural or otherwise, in and about the Building, or any part thereof, and for such purposes to enter upon the Premises, and during the continuance of any of said work, to temporarily close doors, entryways, public space and corridors of the Building and to interrupt or temporarily suspend services and facilities, all without affecting any of Tenant's obligations hereunder, so long as the Premises are reasonably accessible.

(d) To furnish door keys for doors in the Premises at the commencement of the Lease. To retain at all times, and to use in appropriate instances, keys to all doors within and into the Premises. Tenant agrees to purchase only from Landlord additional duplicate keys as required, to change no locks, and not to affix additional locks on doors without the prior written consent of Landlord. Notwithstanding the provisions for Landlord's access to Premises, Tenant relieves the Landlord of all responsibility arising out of theft, robbery, pilferage. Upon the expiration of the Term or Lessee's right to possession, Tenant shall return all keys to Landlord and shall disclose to Landlord the combination of any safes, cabinets or vaults left in the Premises.

(e) To approve the weight, size and location of safes, vaults and other heavy equipment and articles in and about the Premises and the Building (so as not to exceed the legal live load), and to require all such items and furniture and similar items to be moved into or out of the Building and Premises only at such time and in such manner as Landlord shall direct in writing. Tenant shall not install, operate or store any machinery, equipment, mechanical devices, goods, articles or merchandise which may be dangerous to persons or property or which may damage or injure the Premises. Tenant shall not install, operate or store any machinery, equipment, mechanical devices, goods, articles or merchandise which are of a nature not directly related to Tenant's ordinary use of the Premises without the prior written consent of Landlord. Movements of Tenant's property into or out of the Building within the Building are entirely at the risk and responsibility of Tenant and Landlord reserves the right to require permits before allowing any property to be moved into or out of the Building.

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(f) To close the Building after regular working hours and on Saturdays, Sundays and legal holidays subject, however, to Tenant's right to admittance to the Premises under such regulations as Landlord may prescribe from time to time, which may include but shall not be limited to, a requirement that persons entering or leaving the Building identify themselves to a guard or watchman by registration or otherwise and establish their right to enter or leave the Building. Such regulations may include, but shall not be limited to, the requiring of identification from Tenant, Tenant's employees, agents, clients, customers, invitees, visitors and guests.

(g) To establish controls for the purposes of regulating all property and packages (both personal and otherwise) to be moved into or out of the Building and Premises.

(h) To regulate delivery and service of supplies in order to ensure the cleanliness and security of the Premises and to avoid congestion of the loading dock and receiving area.

(i) To show the Premises to prospective tenants at reasonable hours during the last twelve (12) months of the Term and if vacated or abandoned, to show the Premises at any time and to prepare the Premises for reoccupancy.

(j) To erect, use and maintain ducts, conduits, pipes, lines, wiring, drains and flues, and appurtenances thereto, in and through the Premises at reasonable locations.

21. **RULES AND REGULATIONS**. Tenant agrees for itself, its employees, agents, clients, customers, invitees, visitors, and guests, to comply with the current Rules and Regulations for the Building (a copy of which is attached hereto) which, from time to time, may be reasonably modified or supplemented by Landlord. Tenant agrees that Landlord shall not have any duty to Tenant to require other tenants to comply with such Rules and Regulations and Tenant's obligations under this Lease shall not be altered or reduced by reason of Landlord's failure so to do.

22. **LANDLORD'S REMEDIES**. If default shall be made in the payment of the rent or any installment thereof or in the payment of any other sum required to be paid by Tenant under this Lease or under the terms of any other agreement between Landlord and Tenant and such default shall continue for five (5) days after written notice, or if default shall be made in the observance or performance of any of the other covenants or conditions in this Lease which Tenant is required to observe and perform and such shall continue for fifteen (15) days after written notice to Tenant, unless said default cannot be cured within said fifteen (15) days with Tenant using commercially reasonable efforts to so cure and with Tenant having had timely commenced to cure and diligently prosecuting said cure to completion, then such longer period as may be required, or if a default involves a hazardous condition or an insurance obligation and is not cured by Tenant immediately upon written notice to Tenant, or if the interest of Tenant in this Lease shall be levied on under execution or other legal process, or if any voluntary petition in bankruptcy or for corporate reorganization or any similar relief shall be filed by Tenant, or if any involuntary petition in bankruptcy shall be filed against Tenant under any federal or state bankruptcy or insolvency act and shall not have been dismissed within sixty (60) days from the filing thereof, or if a receiver shall be appointed for Tenant or any of the property of Tenant by any court and such receiver shall not have been dismissed within sixty (60) days from the date of his appointment, or if Tenant shall make an assignment for the benefit of creditors, or if Tenant shall admit in writing Tenant's inability to meet Tenant's debts as they mature, or if Tenant shall abandon or vacate the Premises during the Term, then Landlord may treat the occurrence of any one or more of the foregoing events as a breach of this Lease, and thereupon at its option may, with or without notice or demand of any kind to Tenant or any other person, have any one or more of the following described remedies in addition to all other rights and remedies provided at law or in equity or elsewhere herein.

(a) Landlord may terminate this Lease and the Term created hereby, in which event Landlord may forthwith repossess the Premises and be entitled to recover forthwith as damages a sum of money equal to the value of the rent provided to be paid by Tenant for the balance of the original Term, less the fair rental value of the Premises for said period, and any other sum of money and damages owed by Tenant to Landlord. Should the fair rental value exceed the value of the rent provided to be paid by Tenant for the balance or the original Term of the Lease, Landlord shall have no obligation to pay to Tenant the excess or any part thereof.

(b) Landlord may terminate Tenant's right of possession and may repossess the Premises by forcible entry and detainer suit, by taking peaceful possession or otherwise, without demand or notice of any kind to Tenant and without terminating this Lease, in which event Landlord may, but shall be under no obligation to, relet the same for the account of Tenant, for such rent and upon such terms as shall be satisfactory to Landlord. For the purpose of such reletting, Landlord is authorized to decorate or to make any repairs, changes, alterations, or additions in or to the Premises that may be necessary or convenient. If Landlord shall fail to relet the Premises, Tenant shall pay to Landlord as damages a sum equal to the amount of the rental reserved in this Lease for the balance of its original Term. If the Premises are relet and a sufficient sum shall not be realized from such reletting after paying all repairs, changes, alterations and additions and the leasing commissions and other expenses of such reletting and of the collection of the rent accruing therefrom to satisfy the rent provided for in this Lease, Tenant shall satisfy and pay any such deficiency upon demand therefor from time to time. Tenant agrees that Landlord may file suit to recover any sums falling due under the terms of this paragraph from time to time and that no suit or recovery of any portion due Landlord hereunder shall

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be any defense to any subsequent action brought for any amount not theretofore reduced to judgment in favor of Landlord.

Anything in this Section to the contrary notwithstanding, in the event Landlord is entitled to relet the Premises under the provisions hereof, Landlord shall take commercially reasonable steps to attempt to do so.

23. **EXPENSES OF ENFORCEMENT**. The non-prevailing party shall pay upon demand all reasonable costs, charges and expenses including court costs and the reasonable fees of counsel, agents, and others retained incurred in enforcing the obligations hereunder or incurred in any litigation, negotiation or transaction in which one party causes the other, without the other's fault, to become involved or concerned, excluding any negotiations to extend or renew this Lease.

24. **MISCELLANEOUS**.

(a) All rights and remedies of Landlord under this Lease shall be cumulative and none shall exclude any other rights and remedies allowed by law.

(b) All payments becoming due under this Lease and remaining unpaid five (5) days after due will be subject to a One Hundred Fifty and 00/100 Dollars ($150.00) late charge and shall bear interest until paid at the annual rate of three (3%) percent in excess of the Corporate base rate then announced from time to time by Bank One unless a lesser rate shall then be the maximum rate permissible by law with respect thereto, in which event said lesser rate shall be charged. Such late charge and interest shall be deemed Additional Rent hereunder.

(c) The necessary grammatical changes required to make the provisions hereof apply either to corporations or partnerships or individuals, men or women, as the case may require, shall in all cases be assumed as though in each case fully expressed.

(d) Each of the provisions of this Lease shall extend to and shall, as the case may require, bind and inure to the benefit not only of Landlord and of Tenant, but also of their respective heirs, legal representative, successors and assigns, provided this clause shall not permit any assignment by Tenant contrary to the provisions of Paragraph 15 hereof.

(e) Except as otherwise provided, all of the representations and obligations of Landlord are contained herein and in the attached Workletter, and no modification, waiver or amendment of this Lease or of any of its conditions or provisions shall be binding upon the Landlord unless in writing signed by Landlord or by a duly authorized agent of Landlord empowered by a written authority signed by Landlord.

(f) Submissions of this instrument for examination shall not bind Landlord in any manner, and no Lease or obligation of Landlord shall arise until this instrument is signed by Landlord and Tenant and delivery is made to each.

(g) No rights to light or air over any property, whether belonging to Landlord or any other person, are granted to Tenant by this Lease.

(h) At any time hereafter, Landlord may (upon sixty [60] days prior notice) substitute for the Premises other premises in the Complex (herein referred to as the "New Premises") provided that the New Premises shall be similar to the Premises in the area and usable for Tenant's purposes; and if Tenant is already in occupancy of the Premises, then in addition Landlord shall pay the expenses of Tenant's moving from the Premises to the New Premises (including the cost of moving Tenant's telephone equipment and the cost of new stationery) and for improving the New Premises so that they are substantially similar to the Premises. Such move shall be made during evenings, weekends, or otherwise so as to incur the least inconvenience to Tenant.

(i) Tenant acknowledges that Landlord has the right to transfer its interest in the Land and Building and in this Lease, and Tenant agrees that in the event of any such transfer Landlord shall automatically be released from all liability under this Lease and Tenant agrees to look solely to such transferee for the performance of Landlord's obligations hereunder.

(j) The captions of paragraphs are for convenience only and shall not be deemed to limit, construe, affect or alter the meaning of such paragraphs.

(k) Tenant represents and warrants that it is currently in good standing and authorized to do business in the State of Illinois, and Tenant covenants that it shall remain so during the entire Term.

(l) Landlord may terminate this Lease on the last day of any month in any year if Landlord proposes or is required, for any reason, to structurally remodel, remove or demolish the Building or any substantial portion of it. Such termination shall become effective and conclusive by Landlord's written notice to Tenant not less than ninety (90) days prior to the termination date fixed in the notice. No money or other consideration shall be payable by Landlord to Tenant for this right. The right

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hereby reserved by Landlord shall inure to all purchasers, assignees, lessees, transferees and ground or underlying lessee, as the case may be, and is in addition to all other rights of Landlord.

25. **WAIVER OF NOTICE**. Intentionally deleted.

26. **NOTICES**. All notices to be given under this Lease shall be in writing and delivered personally or deposited in the United States mails, certified or registered mail with return receipt requested, postage prepaid, addressed as follows:

(a) If to Landlord: MARC REALTY LLC
c/o Marc Realty
55 E. Jackson Boulevard, Suite 500
Chicago, IL 60604

or such other person at such other address designated by notice sent to Tenant and after occupancy of the Premises by Tenant to the address to which rent is payable.

(b) If to Tenant: UROPARTNERS, LLC

addressed to Tenant at Tenant's present address, and after occupancy of the Premises by Tenant, at 2225 Enterprise Drive, Suite 2511, Westchester, Illinois 60154 or to such other address designated by Tenant in a notice to Landlord.

A notice by mail shall be deemed to have been given two (2) days after deposit in the United States mail as aforesaid.

27. **SECURITY DEPOSIT**. Tenant hereby deposits with Landlord the sum of Six Thousand and 00/100 Dollars ($6,000.00), (hereinafter referred to as "Collateral"), as security for the prompt, full and faithful performance of all obligations of Tenant hereunder.

(a) If Tenant fails to perform any of its obligations hereunder, Landlord may use, apply or retain the whole or any part of the Collateral for the payment of (i) any sum or other sums of money which Tenant may not have paid when due, (ii) any sum expended which Landlord on Tenant's behalf in accordance with the provisions of this Lease; or (iii) any sum which Landlord may expend or be required to expend by reason of Tenant's default, including, without limitation, any damage or deficiency in or from the reletting of the Premises as provided in Paragraph 22. The use, application or retention of the Collateral, or any portion thereof, by Landlord shall not prevent Landlord from exercising any other right or remedy provided by this Lease or by law (it being intended that Landlord shall not first be required to proceed against the Collateral) and shall not operate as a limitation on any recovery to which Landlord may otherwise be entitled. If any portion of the Collateral is used, applied or retained by Landlord for the purposes set forth above, Tenant agrees, within ten (10) days after the written demand therefor is made by Landlord, to deposit cash with the Landlord in an amount sufficient to restore the Collateral to its original amount.

(b) In no event shall the Collateral be deemed to be an advance of payment of rent.

(c) Landlord shall have no obligation to pay any interest on the Collateral.

(d) If the Tenant shall fully and faithfully comply with all of the provisions of this Lease, the Collateral, or any balance thereof, shall be returned to Tenant without interest after the expiration of the Term or upon any later date after which Tenant has vacated the premises. In the absence of evidence satisfactory to Landlord of any permitted assignment of the right to receive the Collateral, or of the remaining balance thereof, Landlord may return the same to the original Tenant, regardless of one or more assignments of Tenant's interest in this Lease or the Collateral. In such event, upon the return of the Collateral, or the remaining balance thereof to the original Tenant, Landlord shall be completely relieved of liability under this Paragraph 27 or otherwise with respect to the Collateral.

(e) Tenant acknowledges that Landlord has the right to transfer its interest in the Land and Building and in this Lease and Tenant agrees that in the event of any such transfer, Landlord shall have the right to transfer the Collateral to the transferee. Upon the delivery by Landlord to Tenant of such transferee's written acknowledgment of its receipt of such Collateral, Landlord shall thereby be released by Tenant from all liability or obligation for the return of such Collateral and Tenant agrees to look solely to such transferee for the return of the Collateral.

(f) The Collateral shall not be mortgaged, assigned or encumbered in any manner whatsoever by Tenant without the prior written consent of Landlord.

In addition to the Collateral, Tenant shall furnish Landlord, upon execution hereof, an irrevocable Letter of Credit ("LC") for the benefit of Landlord for the Term of this Lease and in the initial amount of Seventy-Five Thousand and 00/100 Dollars ($75,000.00). Landlord may draw upon the LC in the event of a default by Tenant in the payment of any Rent or other sums due under this Lease or on account of Tenant's failure to renew an expiring LC as set forth below. The LC shall be issued by a United States bank

ATTACHMENT 2
Site Ownership

reasonably satisfactory to Landlord with offices in downtown Chicago which office will accept and pay the LC. The LC shall provide that (i) it may be drawn upon solely and unilaterally by Landlord by Landlord delivering a statement certified by Landlord that Landlord is entitled to draw on the LC in the amount being demanded by Landlord; and (ii) the funds under the LC shall be immediately available to Landlord after delivery of the above statement, without any other documentation required or other review period of the issuer. The initial LC shall be valid for twelve (12) full calendar months and shall be renewed for each consecutive twelve (12) month period throughout the Term of this Lease on no later than sixty (60) days prior to the expiration of each consecutive twelve (12) month period. The amount of the LC may be reduced to Fifty Thousand and 00/100 Dollars ($50,000.00) after Tenant has paid to Landlord its twelfth (12th) installment of monthly Base Rent; reduced to Twenty-Five Thousand and 00/100 Dollars ($25,000.00) after Tenant has paid to Landlord its twenty-fourth (24th) installment of monthly Base Rent; and finally reduced to zero ($0.00) after Tenant has paid to Landlord its thirty-sixth (36th) installment of monthly Base Rent.

28. **REAL ESTATE BROKER**. The Tenant represents that the Tenant has dealt only with MARC REALTY, as broker, in connection with this Lease, and that insofar as the Tenant knows, no other broker negotiated this Lease or is entitled to any commission in connection therewith.

29. **COVENANT OF QUIET ENJOYMENT**. The Landlord covenants that the Tenant, on paying the Base Rent, applicable Additional Rent, charges for services and other payments herein reserved, and, on keeping, observing and performing all the other terms, covenants, conditions, provisions and agreements herein contained on the part of the Tenant to be kept, observed, and performed, shall, during the Term, peaceably and quietly have, hold and enjoy the Premises subject to the terms, covenants, conditions, provisions, and agreements hereof.

30. **LIMITED PERSONAL GUARANTY**. Intentionally deleted.

31. **OPTION TO TERMINATE**. Tenant shall have the right to terminate this Lease, said termination to be effective November 30, 2008, provided:

(a) Tenant is not then in default of any of the terms and conditions of this Lease and this Lease is then in full force and effect;

(b) Landlord receives written notice from Tenant exercising this option not later than March 1, 2008; and

(c) Tenant delivers to Landlord, together with the above notice, a termination fee (the "Fee") consisting of (i) the unamortized amount of all brokers commissions Landlord incurred relative to this Lease and (ii) the undepreciated build-out costs Landlord incurred relative to this Lease, each amortized/depreciated over the original rental stream of this Lease at 9% interest thereon; plus an amount equal to three (3) months of the then monthly Base Rent.

In the event the entire Fee is not delivered to Landlord by Tenant together with the above Notice, Tenant's exercise of this option shall be null and void and of no force or effect.

32. **WAIVER OF JURY TRIAL AND COUNTERCLAIM**. Tenant hereby waives trial by jury in any action or proceeding brought by Landlord on any possession matters or monetary matters whatsoever arising out of or in any way connected with the payment of monthly Base Rent or Additional Rent. In the event Landlord commences any proceedings for possession or nonpayment of any rent, Tenant will not interpose any counterclaim (except compulsory counterclaims) of whatever nature or description in any such proceedings. This shall not, however, be construed as a waiver of the Tenant's right to assert such claims in any separate action or actions brought by the Tenant.

IN WITNESS WHEREOF, Landlord and Tenant have caused this Lease to be duly executed as of the day and year first above written.

LANDLORD:	TENANT:
MARC REALTY LLC, as Managing Agent aforesaid	**UROPARTNERS, LLC,** an Illinois limited liability company
By:______________________ Manager	By:______________________ Manager

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Uropartners_2.doc 08/16/2005

ATTACHMENT 2
Site Ownership

RULES AND REGULATIONS

1. The sidewalks, entrances, passages, concourses, ramps, courts, elevators, vestibules, stairways, corridors, or halls shall not be obstructed or used by Tenant or the employees, agents, servants, visitors or business of Tenant for any purpose other than ingress and egress to and from the Premises and for delivery of merchandise and equipment in prompt and efficient manner, using elevators and passageways designated for such delivery by Landlord.

2. No awnings, air-conditioning units, fans or other projections shall be attached to the Building. No curtains, blinds, shades, or screens shall be attached to or hung in, or used in connection with, any window or door of the Premises or Building, without the prior written consent of Landlord. All curtains, blinds, shades, screens or other fixtures must be of a quality type, design and color, and attached in the manner approved by Landlord. All electrical fixtures hung in offices or spaces along the perimeter of the Premises must be fluorescent, of a quality, type, design and bulb color approved by Landlord unless the prior consent of Landlord has been obtained for other lamping.

3. No sign, advertisement, notice or other lettering shall be exhibited, inscribed, painted or affixed by any Tenant on any part of the outside of the Premises or Building or on the inside of the Premises if the same can be seen from the outside of the Premises without the prior written consent of Landlord. In the event of the violation of the foregoing by Tenant, Landlord may remove same without any liability, and may charge the expense incurred by such removal to the Tenant or Tenants violating this rule. Interior signs on doors and the directory shall be inscribed, painted or affixed for each Tenant by Landlord at the expense of such Tenant, and shall be of a standard size, color and style acceptable to Landlord.

4. The exterior windows and doors that reflect or admit light and air into the Premises or halls, passageways or other public places in the Building, shall not be covered or obstructed by any Tenant, nor shall any articles be placed on the windowsills. No showcases or other articles shall be put in front or affixed to any part of the exterior of the Building, nor placed in the halls, corridors or vestibules, nor shall any article obstruct any HVAC supply or exhaust equipment without the prior written consent of Landlord.

5. The electrical and mechanical closets, water and wash closets, drinking fountains and other plumbing and electrical and mechanical fixtures shall not be used for any purposes other than those for which they were constructed, and no sweepings, rubbish, rags, coffee grounds, acids or other substances shall be deposited therein. All damages resulting from any misuse of the fixtures shall be borne by the Tenant who, or whose servants, employees, agents, visitors or licensees, shall have caused the same. No person shall waste water by interfering or tampering with the faucets or otherwise.

6. No portion of the Premises or the Building shall be used or occupied at any time for manufacturing, for the storage of merchandise, for the sale of merchandise, goods or property of any kind at auction or otherwise or as a sleeping or lodging quarters.

7. Tenant, any Tenant's servants, employees, agents, visitors or licensees, shall not at any time bring or keep upon the Premises any inflammable, combustible, caustic, poisonous or explosive fluid, chemical or substance except as otherwise set forth in the Lease.

8. Tenant, any Tenant's servants, employees, agents, visitors or licensees, shall not at any time bring or keep upon the Premises any weapons including but not limited to handguns, rifles and knives.

9. No bicycles, vehicles or animals of any kind (other than a seeing eye dog for a blind person), shall be brought into or kept by any Tenant in or about the Premises or the Building.

10. Tenant shall not use or occupy or permit any portion of the Premises to be used or occupied as an office for a public stenographer or typist, offset printing, or for the possession, storage, manufacture or sale of liquor, drugs, tobacco in any form or as a barber or manicure shop, an employment bureau, a labor office, a dance or music studio, any type of school, or for any use other than those specifically granted in the lease. Tenant shall not engage or pay any employees on the Premises, except those actually working for such Tenant on said Premises, and Tenant shall not advertise for labor giving an address at said Premises.

11. Landlord shall have the right to prohibit any advertising by any Tenant which, in Landlord's opinion, tends to impair the reputation of the Building or its desirability as a building for offices, and upon written notice from Landlord, Tenant shall refrain from or discontinue such advertising. In no event shall Tenant, without the prior written consent of Landlord, use the name of the Building or use pictures or illustrations of the Building.

12. Any person in the Building will be subject to identification by employees and agents of Landlord. All persons in or entering Building shall be required to comply with the security policies of the Building. Tenant shall keep doors to unattended areas locked and shall otherwise exercise reasonable precautions to protect property from theft, loss, or damage. Landlord shall not be responsible for the theft, loss, or damage of any property.

13. No additional locks or bolts of any kind shall be placed on any door in the Building or the Premises and no lock on any other door therein shall be changed or altered in any respect without the written consent of Landlord, except to secure Tenant's lab chemicals. Landlord shall furnish two keys for each lock on exterior doors to the Premises and shall, on Tenant's request and at Tenant's expense, provide additional duplicate keys. All keys, including keys to storerooms and bathrooms, shall be returned to Landlord upon termination of this Lease.

ATTACHMENT 2
Site Ownership

Landlord may at all times keep a pass key to the Premises. All entrance doors to the Premises shall be left closed at all times, and left locked when the Premises are not in use.

14. Tenant shall give immediate notice to Landlord in case of theft, unauthorized solicitation, or accident in the Premises or in the Building or of defects therein or in any fixtures or equipment, or of any known emergency in the Building.

15. Tenant shall not use the Premises or permit the Premises to be used for photographic, multilith or multigraph reproductions except in connection with its own business and not as a service for others, without Landlord's prior permission.

16. No freight, furniture or bulky matter of any description will be received into the Building or carried into the elevators except in such a manner, during such hours and using such elevators and passageways as may be approved by Landlord, and then only upon having been scheduled at least two (2) working days prior to the date on which such service is required. Any hand trucks, carryalls, or similar appliances used for the delivery or receipt of merchandise or equipment shall be equipped with rubber tires, side guards and such other safeguards as Landlord shall require.

17. Tenants, or the employees, agents, servants, visitors or licensees of Tenant shall not at any time or place leave or discard any rubbish, paper, articles or objects of any kind whatsoever outside the doors of the Premises or in the corridors or passageways of the Buildings.

18. Tenant shall not make excessive noises, cause disturbances or vibrations or use or operate any electrical or mechanical devices that emit excessive sound or other waves or disturbances or create obnoxious odors, any of which may be offensive to the other tenants and occupants of the Building, or that would interfere with the operation of any device, equipment, radio, television broadcasting or reception from or within the Building or elsewhere and shall not place or install any projections, antennas, aerials or similar devices inside or outside of the Premises or on the Building without Landlord's prior written approval.

19. Tenant shall comply with all applicable federal, state and municipal laws, ordinances and regulations, insurance requirements and building rules and regulations and shall not directly or indirectly make any use of the Premises which may be prohibited by any of the foregoing or which may be dangerous to persons or property or may increase the cost of insurance or require additional insurance coverage.

20. Tenant shall not serve, nor permit the serving of alcoholic beverages in the Premises unless Tenant shall have procured Host Liquor Liability insurance, issued by companies and in amounts reasonably satisfactory to Landlord, naming Landlord as an additional insured.

21. The requirements of Tenant will be attended to only upon written application at the Office of the Building. Employees shall not perform any work or do anything outside of the regular duties unless under special instructions from the Office of the Building.

22. Canvassing, soliciting and peddling in the Building is prohibited and Tenant shall cooperate to prevent the same.

23. Except as otherwise explicitly permitted in its Lease, Tenant shall not do any cooking, conduct any restaurant, luncheonette or cafeteria for the sale or service of food or beverages to its employees or to others, install or permit the installation or use of any food, beverage, cigarette, cigar or stamp dispensing machine or permit the delivery of any food or beverage to the Premises, except by such persons delivering the same shall be approved by Landlord.

24. Tenant shall at all times keep the Premises neat and orderly.

25. Tenant, its servants, employees, customers, invitees and guests shall, when using the parking facilities in and around the building, observe and obey all signs regarding fire lanes, handicapped and no parking, or otherwise regulated parking zones, and when parking always park between the designated lines. Landlord reserves the right to tow away, at the expense of the owner, any vehicle which is improperly parked or parked in violation of a posted regulation. All vehicles shall be parked at the sole risk of the owner, and Landlord assumes no responsibilities for any damage to or loss of vehicles.

26. Tenants, and the employees, agents, servants, visitors or licensees of Tenant shall, at all times, conduct themselves in a businesslike manner.

27. Tenant shall not allow and shall use its best efforts to prevent its employees, customers, or invitees from loitering in the common areas of the Building or from disturbing, in any manner, the business operations of any other tenant of the Building.

28. In accordance with the Illinois Indoor Clean Air Act, no smoking is permitted in the common areas, including the atrium, or within twenty (20) feet of any of entrance or exit door to the Building or any tenant's suite.

ATTACHMENT 2
Site Ownership

ENTERPRISE CENTER

WORKLETTER

Gentlemen:

This is the Workletter referred to in the foregoing Lease (the "Lease") wherein you ("Tenant") lease certain space from the MARC REALTY LLC, ("Landlord") in the Office Building at 2205-2255 Enterprise Drive, Westchester, Illinois 60154. The words "Premises," "Building," and "Term" as used herein shall have the respective meanings assigned to them in the Lease.

Landlord and Tenant agree as follows:

1. WORK

Landlord, at Landlord's sole cost and expense not to exceed Twenty Thousand Six Hundred Twenty and 00/100 Dollars ($20,620.00, "Landlord's Allowance") and thereafter at Tenant's sole cost and expense ("Tenant's Contribution") (such Landlord's Allowance and Tenant's Contribution, collectively, "Tenant Improvement Cost"), using Building standard materials and workmanship, shall do the things in the Premises (hereinafter called the "Work") which are provided for in Space Plan #:SP-1R dated 8/5/2005 attached hereto. Tenant shall be responsible for the cost of any changes made to the Space Plan or any additional work added after the date of approval of the Space Plan by Landlord in excess of the Landlord's Allowance. Subject to the provisions of the Lease and to the provisions of this Workletter, Landlord shall proceed diligently to cause the Work to be substantially completed at or before the commencement of the Term. Tenant Improvement Costs shall be defined to include all design fees (including but not limited to space planning fees, design fees, engineering fees), construction labor and materials, and the industry standards for construction contractor's overhead and fees. Tenant Improvement Costs shall not include furniture or equipment of any kind (including telecommunications equipment). Tenant shall reimburse Landlord for any monies expended by Landlord pursuant to this Paragraph for the cost of any work outside of the scope of the approved work, and such amounts must be paid by the Tenant to Landlord within ten (10) days after Landlord sending Tenant written demand for same.

Landlord's initial estimate of the amount of Tenant's Contribution is $53,845.00, of which Tenant shall pay to Landlord one-half (1/2, $26,922.00) prior to commencement of the Work. The remaining balance thereof, subject to adjustment based upon the actual cost of such Tenant's Contribution, shall be due and payable within thirty (30) days after substantial completion of the Work.

2. ADDITIONAL WORK

If Tenant wishes, Landlord, prior to the commencement of the Term to do any construction, decorating or similar things in the Premises in addition to the Work to be performed by Landlord pursuant to Paragraph 1 hereof (the "Additional Work") Tenant may, at its expense, submit drawings and specifications for the Additional Work (the "Additional Plans") to Landlord for its approval. Landlord shall have no duty to approve the same or to do or permit any Additional Work and shall not be deemed to have done so unless it approves the same in writing or agrees in writing to do or permit such Additional Work. If Landlord agrees to do so, it shall submit to Tenant estimates of the cost thereof. Within seven (7) days after receipt of such estimate, Tenant shall either direct Landlord in writing to do the Additional Work at Tenant's cost or Tenant shall be deemed to have abandoned its request for such Additional Work. Tenant agrees to pay to Landlord within seven (7) days after receipt of bills therefore (which bills may be rendered by Landlord from time to time during the course of such Additional Work or any time) the cost of all such Additional Work (without regard to whether such cost exceeds the estimates furnished) together with fifteen (15%) percent of said cost for Landlord's overhead.

It is understood that any additions or alterations to the Premises desired by Tenant after the commencement of the Term shall be subject to the provisions of Paragraph 8 of the Lease.

ATTACHMENT 2
Site Ownership

3. SUBSTITUTIONS AND CREDITS

Tenant may select other available materials in place of Building Standard materials (which are defined as those materials designated by Landlord, at its option, for general use in the Building) provided that such selection is approved in writing by Landlord and that such other materials constitute a "substitution in kind" as hereinafter described. Landlord shall have no duty to approve any proposed substitution. Tenant agrees to pay to Landlord within seven (7) days after receipt of bills therefore (which bills may be rendered by Landlord from time to time during the course of the Work or any time) an amount equal to the excess of the Landlord's cost for acquiring and installing such substituted materials over the cost which Landlord would have incurred in acquiring and installing the Building Standard materials that were replaced thereby plus fifteen (15%) percent of such excess shall be final and binding upon Tenant. Credit shall be granted only to the extent of substitutions in kind. For example, a lighting fixture credit may be applied only against the cost of another lighting fixture and an electrical outlet credit may not be applied against the cost of bank screen partitions.

4. ACCESS BY TENANT PRIOR TO COMMENCEMENT OF TERM

Landlord, at Landlord's discretion, may permit Tenant and Tenant's agents, suppliers, contractors and workmen to enter the Premises prior to the commencement of the Term to enable Tenant to install carpeting or do such other things as may be required by Tenant to make the Premises ready for Tenant's occupancy. Tenant agrees that if such permission is granted Tenant and its agents, contractors, workmen, and suppliers and their activities in the Premises and Building will not interfere with or delay the completion of the Work or Additional Work to be done by Landlord and will not interfere with other activities of Landlord or occupants of Building. Landlord shall have the right to withdraw such permission upon twenty-four (24) hours written notice to Tenant if Landlord determines that any such interference or delay has been or may be caused. Tenant agrees that any such entry into the Premises shall be at Tenant's own risk and Landlord shall not be liable in any way for any death or injury to any person and for any injury, loss or damage which may occur to any of Tenant's property or installation made in the Premises and Tenant agrees to protect, defend, indemnify and save harmless Landlord from all liabilities, costs, damages, fees and expenses arising out of or connected with the activities of Tenant or its agents, contractors, suppliers or work men in or about the Premises or Building.

LANDLORD:

MARC REALTY LLC,
as Managing Agent aforesaid

By:_____
Manager

TENANT:

UROPARTNERS, LLC,
an Illinois limited liability company

By:_____
Manager

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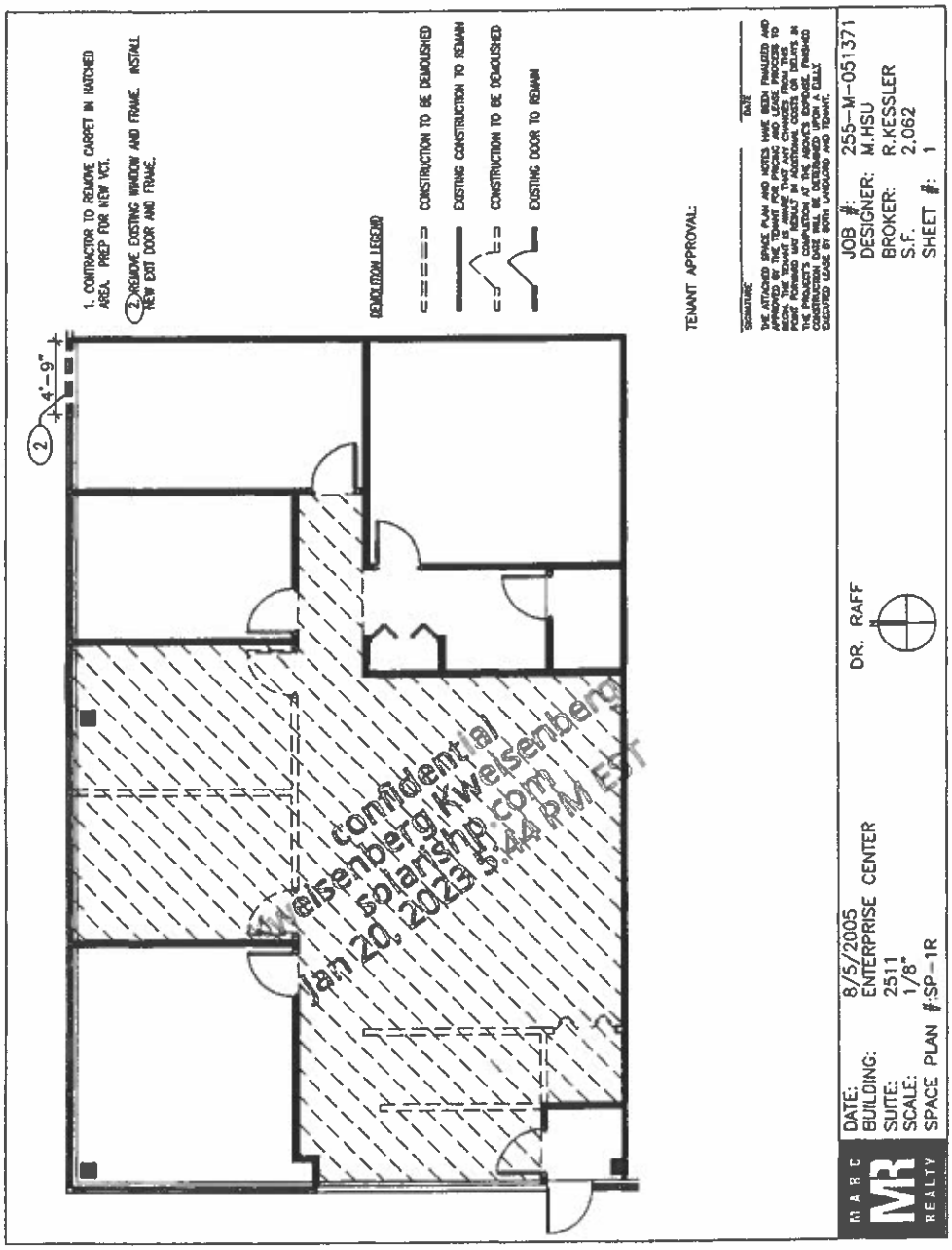
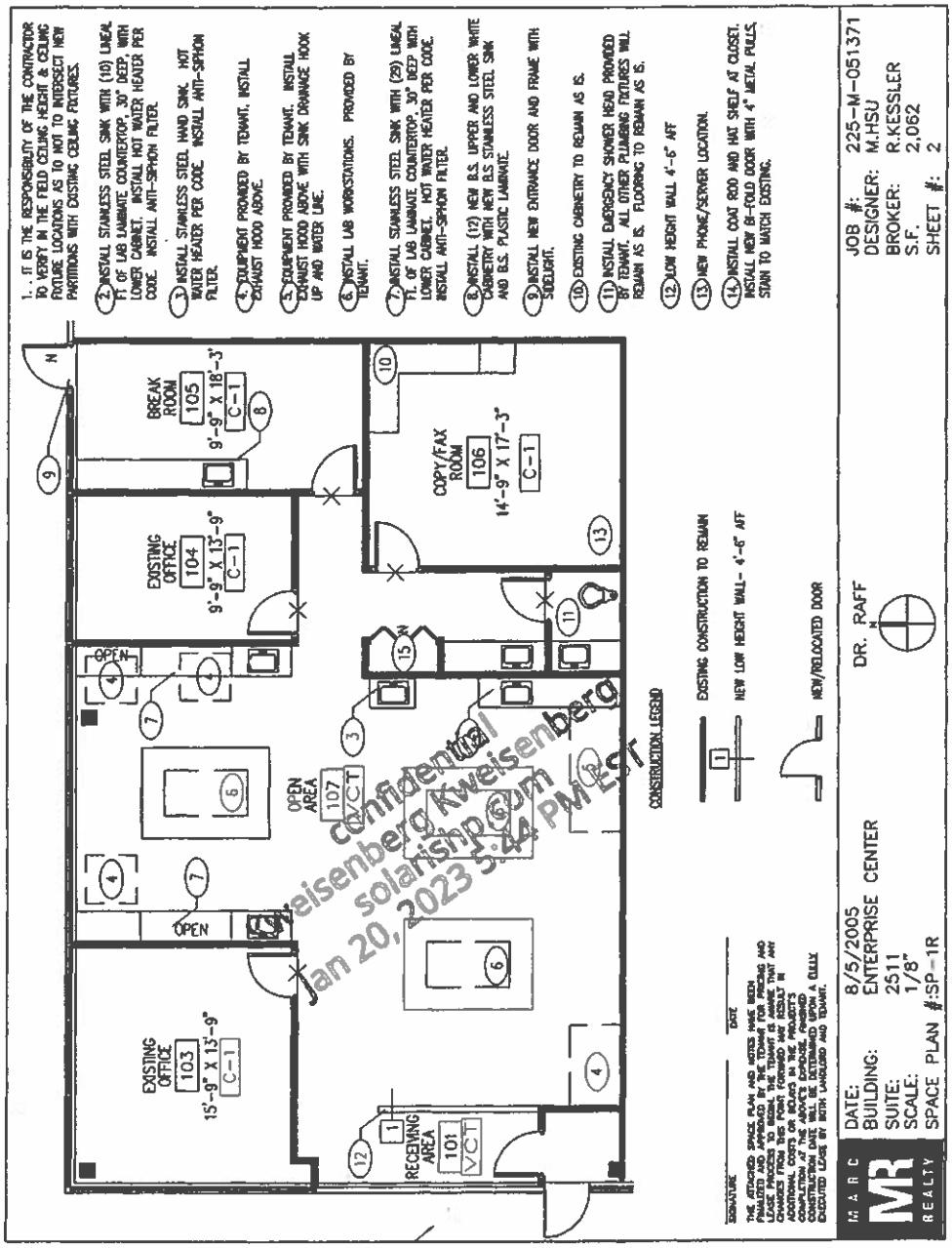
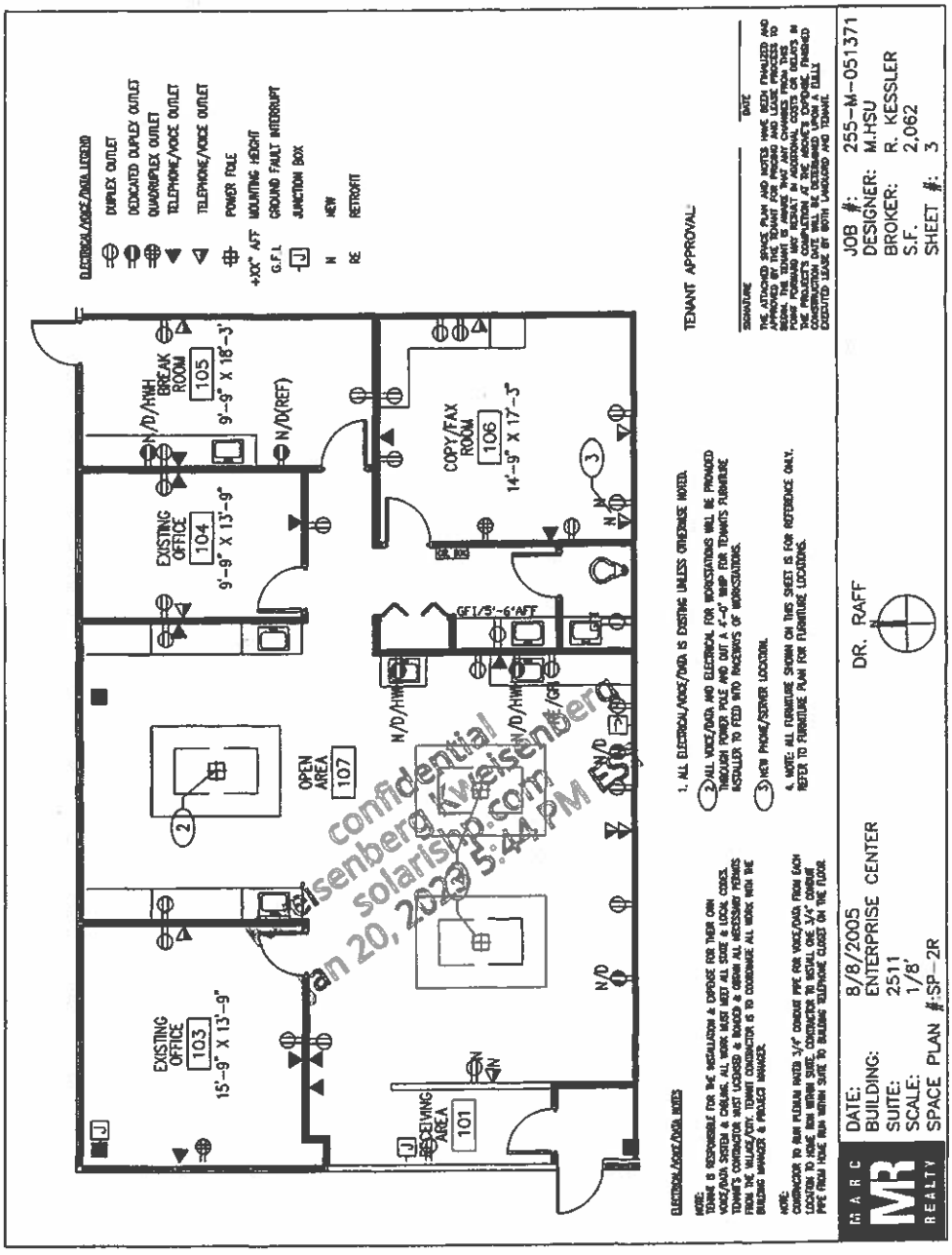
ATTACHMENT 2
Site Ownership



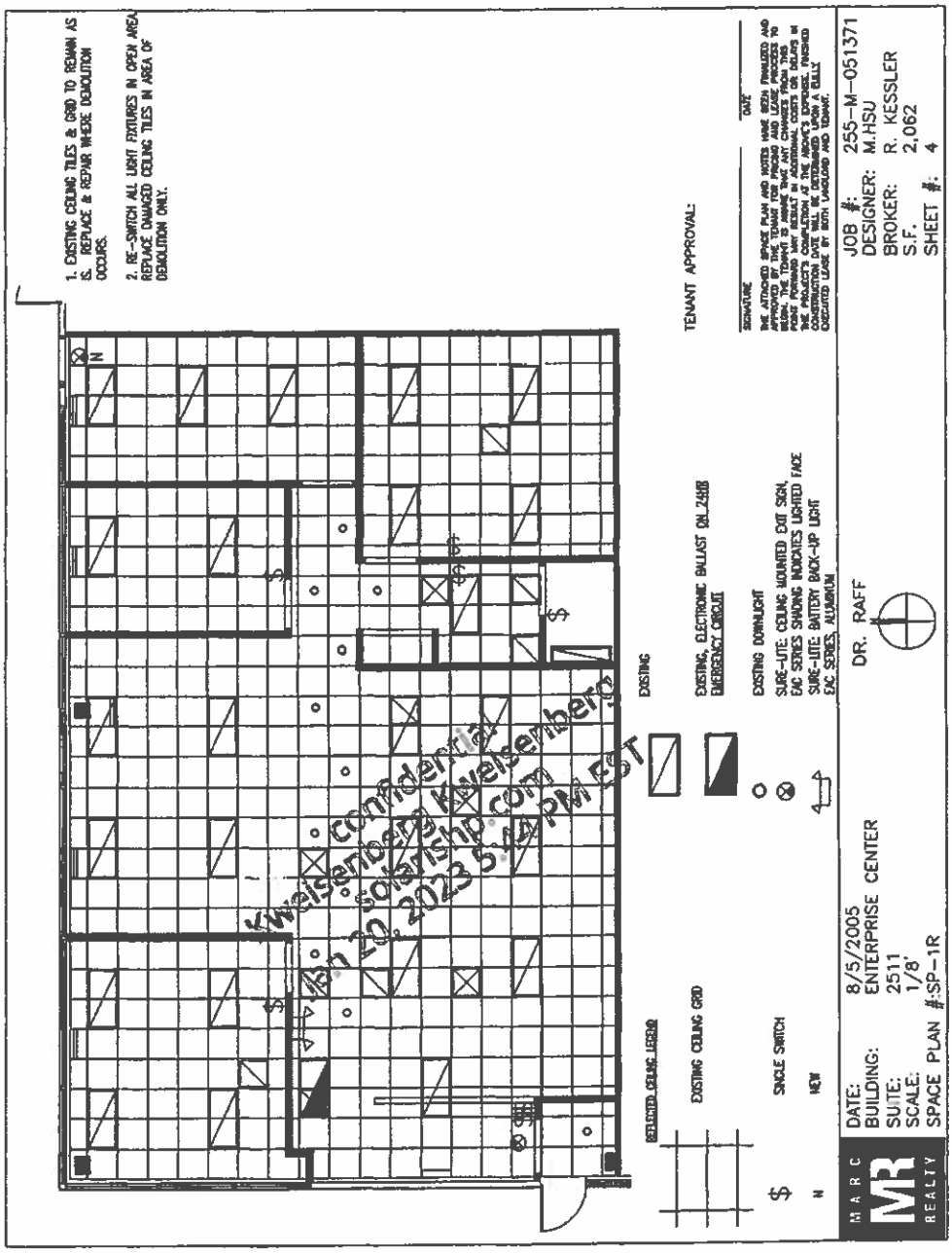
ATTACHMENT 2
Site Ownership



ATTACHMENT 2
Site Ownership



ATTACHMENT 2
Site Ownership



ATTACHMENT 3
Facility Ownership

The lab will continue to operate as UroPartners Imaging Center, which is owned and operated by UroPartners, LLC.

Following the modernization and acquisition of medical equipment, the ownership of the facility shall remain unchanged and there will be no other changes to the existing ownership structure or operation of the Imaging Center. Included with this Attachment is the facility owner's Certificate of Good Standing.

File Number 0142447-5

STATE OF ILLINOIS
OFFICE OF
THE SECRETARY OF STATE

To all to whom these Presents Shall Come, Greeting:

I, **Alexi Giannoulias,** *Secretary of State of the State of Illinois, do hereby certify that I am the keeper of the records of the Department of Business Services. I certify that*

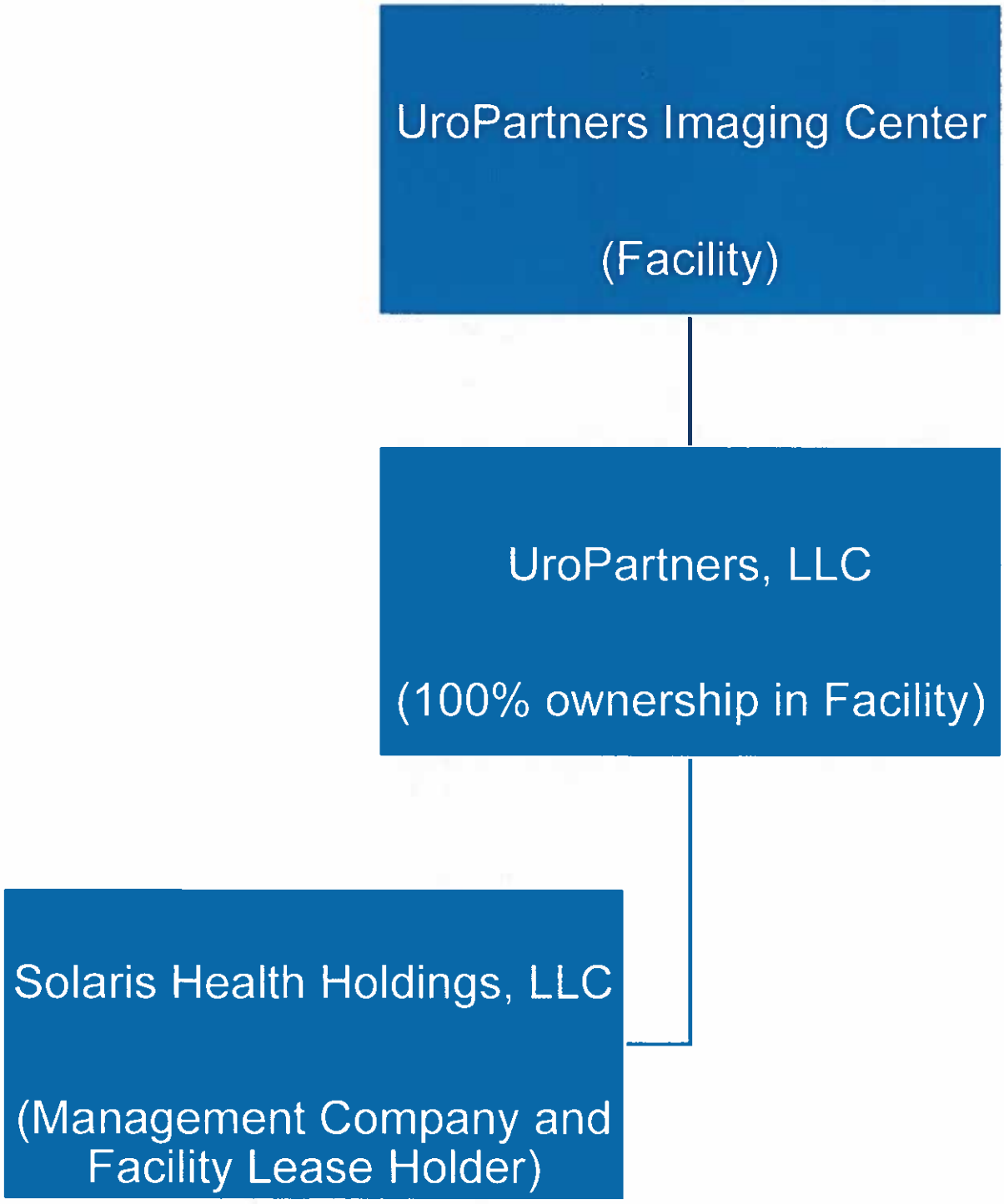
UROPARTNERS, LLC, HAVING ORGANIZED IN THE STATE OF ILLINOIS ON FEBRUARY 10, 2005, APPEARS TO HAVE COMPLIED WITH ALL PROVISIONS OF THE LIMITED LIABILITY COMPANY ACT OF THIS STATE, AND AS OF THIS DATE IS IN GOOD STANDING AS A DOMESTIC LIMITED LIABILITY COMPANY IN THE STATE OF ILLINOIS.

In Testimony Whereof, *I hereto set my hand and cause to be affixed the Great Seal of the State of Illinois, this* 31ST *day of* MARCH *A.D.* 2025 .

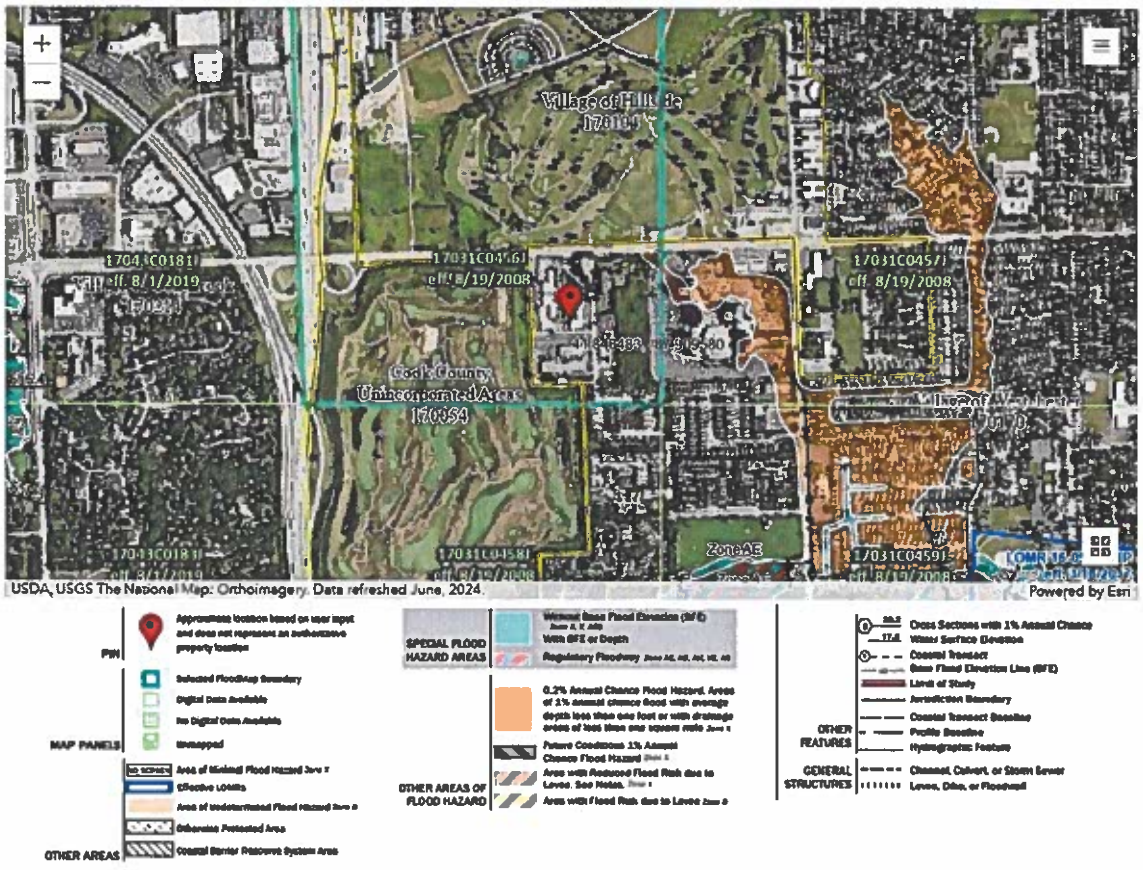
Authentication #: 2509004334 verifiable until 03/31/2026
Authenticate at: https://www.ilsos.gov

SECRETARY OF STATE

ATTACHMENT 4
Site Ownership



ATTACHMENT 5
Flood Plain Map



ATTACHMENT 5
Flood Plain Requirements

June 2, 2025

John P. Kniery
Board Administrator
Illinois Health Facilities and Services Review Board
525 W Jefferson Street, Floor 2
Springfield, IL 62761

Re: UroPartners Pathology Lab - Flood Plain Requirements

Dear Mr. Kniery:

As representative of UroPartners, LLC, I, Daniel Scharff, affirm that our facility complies with Illinois Executive Order #2005-5. The facility located at 2225 Enterprise Drive, Suite 2511 Westchester, Illinois 60154 is not located in a flood plain, as evidence please find enclosed a map from the Federal Emergency Management Agency ("FEMA").

I hereby certify this true and is based upon my personal knowledge under penalty of perjury and in accordance with 735 ILCS 5/1-109.

Sincerely,

Daniel Scharff
Secretary
UroPartners, LLC

ATTACHMENT 6
Historical Preservation Letter

The applicant submitted a request for determination to the Illinois Department of Natural Resources-Preservation Services Division on May 27, 2025. A final determination has been received and is included with this attachment.

ATTACHMENT 6
Historical Preservation Letter

Cook County
Westchester
CON - Acquisition of Major Medical Equipment
2225 Enterprise Dr., Suite 2511

IHFSRB, SHPO Log #009052225

May 28, 2025

Juan Morado
Benesch, Friedlander, Coplan and Aronoff LLP
71 S. Wacker Dr., Suite 1600
Chicago, IL 60606

This letter is to inform you that we have reviewed the information provided concerning the referenced project. Our review of the records indicates that no historic, architectural exist within the project area. Our office did not conduct an archaeological review because no ground disturbing activity is included in the application.

A previous letter, dated 5/23/25, from our office reviewed another address in Des Plaines, but the application included an incorrect address. This current letter covers the correct address.

Please retain this letter in your files as evidence of compliance with Section 4 of the Illinois State Agency Historic Resources Preservation Act (20 ILCS 3420/1 et. seq.). This clearance remains in effect for two years from date of issuance. It does not pertain to any discovery during construction, nor is it a clearance for purposes of the Illinois Human Remains Protection Act (20 ILCS 3440).

If you have any further questions, please contact Steve Dasovich, Cultural Resources Manager, at 217/782-7441 or at Steve.Dasovich@illinois.gov.

Sincerely,

Carey L. Mayer

Carey L. Mayer, AIA
Deputy State Historic Preservation Officer

ATTACHMENT 6
Historical Preservation Letter

Benesch

Juan Morado, Jr.
71 South Wacker Drive, Suite 1600
Chicago, Illinois 60606-4637
Direct Dial: 312.212.4967
Fax: 312.767.9192
jmorado@beneschlaw.com

May 27, 2025

VIA E-MAIL

Jeffrey Kruchten
Chief Archaeologist
Preservation Services Division
Illinois Historic Preservation Office Illinois Department of Natural Resources
1 Natural Resources Way
Springfield, IL 62702
SHPO.Review@illinois.gov

Re: Certificate of Need Application for Acquisition of Major Medical Equipment

Dear Jeffrey:

I am writing on behalf of my client, UroPartners Pathology Lab ("UroPartners") to request a review of the project area under Section 4 of the Illinois State Agency Historic Resources Preservation Act (20 ILCS 3420/1 et. seq.). UroPartners is submitting an application for a Certificate of Need from the Illinois Health Facilities and Services Review Board due to a service modernization. In particular, UroPartners intends to acquire major medical equipment for its pathology lab at 2225 Enterprise Drive, Suite 2511 Westchester, Illinois 60154, including a Positive Emission Tomography-Computed Tomography scan machine, fixed artis ceiling, and an ultrasound.

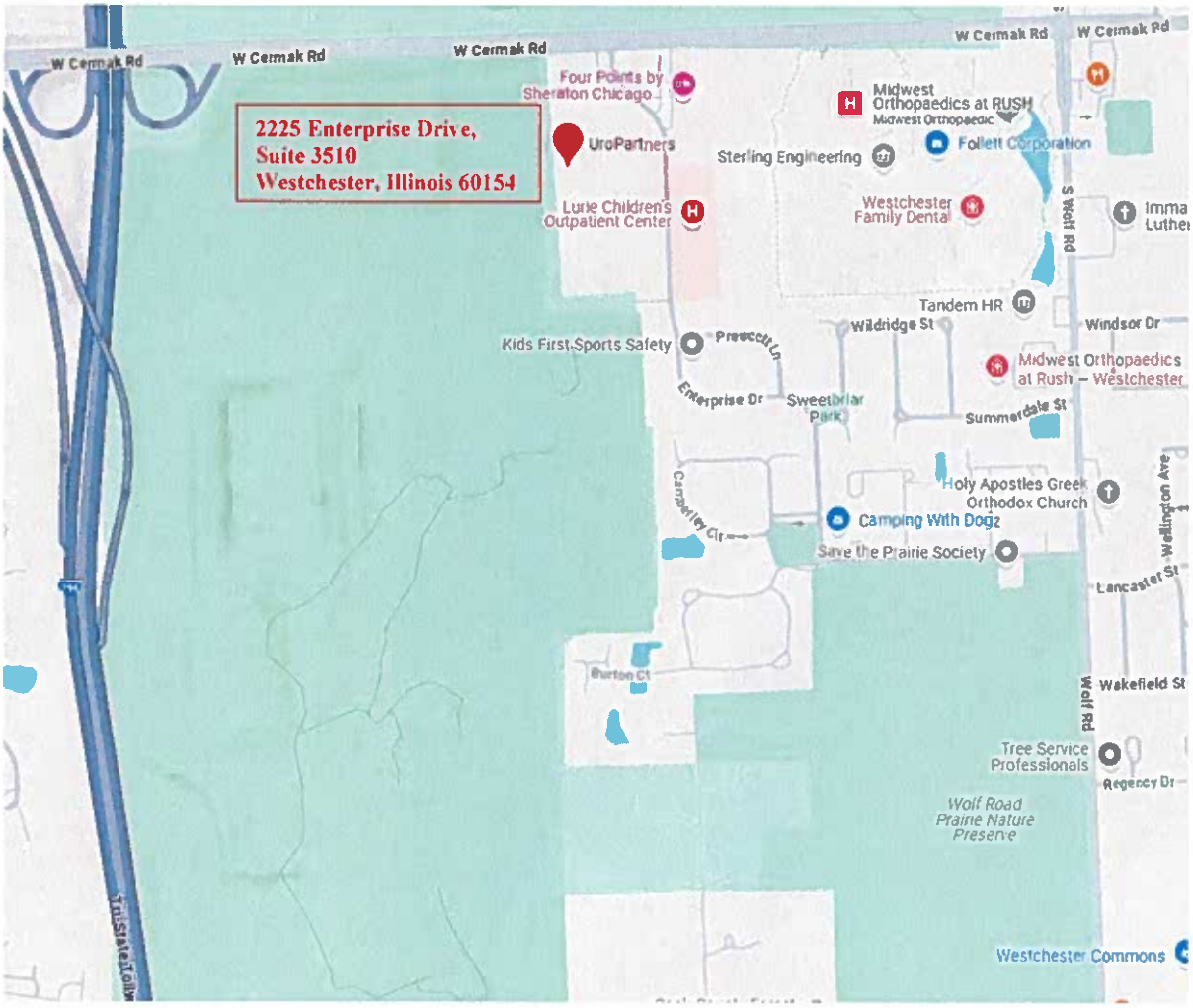
For your reference, we have enclosed pictures of the existing lot and topographic maps showing the general location of the project. We respectfully request review of the project area and a determination letter at your earliest convenience. Thank you in advance for all of the time and effort that will be going into this review.

Very truly yours,

BENESCH, FRIEDLANDER,
COPLAN & ARONOFF LLP

Juan Morado, Jr.

ATTACHMENT 6
Historical Preservation Letter
Topographic Map (2225 Enterprise Drive, red pinpoint)



ATTACHMENT 6
Historical Preservation Letter
3D Aerial Map of 2225 Enterprise Drive, Suite 3510 Westchester, Illinois 60154

ATTACHMENT 6
Historical Preservation Letter
Street View of 2225 Enterprise Drive, Suite 3510 Westchester, Illinois 60154

ATTACHMENT 6
Historical Preservation Letter
Aerial View of 2225 Enterprise Drive Westchester, Illinois 60154

ATTACHMENT 7
Project Costs and Sources of Funds

Project Costs and Sources of Funds			
USE OF FUNDS	**CLINICAL**	**NONCLINICAL**	**TOTAL**
Preplanning Costs	-	-	-
Site Survey and Soil Investigation	-	-	-
Site Preparation	-	-	-
Off Site Work	-	-	-
New Construction Contracts	$1,715,991	$807,525	$2,523,516
Modernization Contracts	-	-	-
Contingencies	$170,000	$80,000	$250,000
Architectural/Engineering Fees	$148,620	$99,080	$247,700
Consulting and Other Fees	$100,000	$100,000	$200,000
Movable or Other Equipment (not in construction contracts)	$1,620,587	$762,629	$2,383,216
Bond Issuance Expense (project related)	-	-	-
Net Interest Expense During Construction (project related)	-	-	-
Fair Market Value of Leased Space or Equipment	-	-	-
Other Costs To Be Capitalized	$101,166	$47,608	$148,774
Acquisition of Building or Other Property (excluding land)	-	-	-
TOTAL USES OF FUNDS	$3,856,364	$1,896,842	$5,753,206
SOURCE OF FUNDS	**CLINICAL**	**NONCLINICAL**	**TOTAL**
Cash and Securities	$3,856,364	$1,896,842	$5,753,206
Pledges	0	0	0
Gifts and Bequests	0	0	0
Bond Issues (project related)	0	0	0
Mortgages	0	0	0
Leases (fair market value)	0	0	0
Governmental Appropriations	0	0	0
Grants	0	0	0
Other Funds and Sources	0	0	0
TOTAL SOURCES OF FUNDS	$3,856,364	$1,896,842	$5,753,206

ATTACHMENT 7
Project Costs and Sources of Funds

New Construction Contracts - The project building costs are based on national architectural and construction standards and adjusted to compensate for several factors. While specific recent data for Chicagoland is limited, industry reports indicate that construction costs in the region remain higher than the national average, though the rate of increase has slowed. For example, a 2025 report from Rider Levett Bucknall notes a national year-over-year construction cost increase of 4.35% in Q1 2025, down from 5.86% in the same period in 2024. Coupled with the unexpected increases in labor and raw material costs due to the COVID-19 pandemic, the project's costs are higher than originally planned but are consistent with UroPartners' experience in purchasing similar equipment and installing it in their facilities. The clinical construction costs are estimated to be $1,715,991 or $461.41 per clinical square foot.

Contingencies - The Project's contingencies costs are designed to allow the construction team an amount of funding for unforeseeable event related to construction. Clinical construction costs for contingencies are estimated to be $170,000 or 9.9% percent of projected clinical new construction costs.

Architectural/Engineering Fees - The clinical project cost for architectural/engineering fees are projected to be $148,620 or 7.8% of the new construction and contingencies costs.

Consulting and Other Fees - The Project's consulting fees are primarily comprised of various project related fees, additional state/local fees, and other CON related costs.

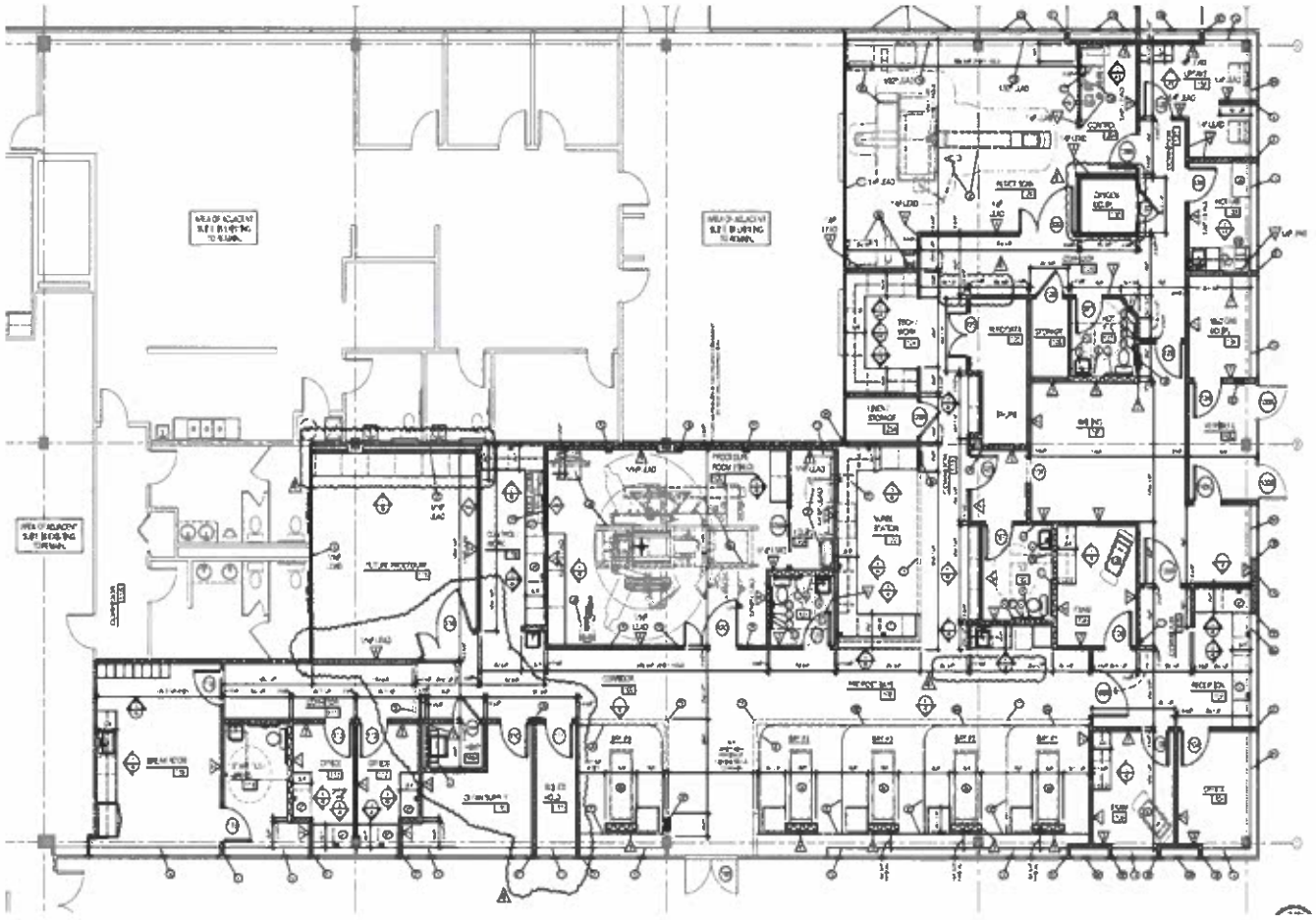
Moveable Equipment Costs - The moveable equipment costs are necessary for the operation of the observation unit and renovation of the ultrasound room.

PET CT Machine	$1,088,936
Fixed Art Ceiling	$769,580
Mobile Cios Spin	$484,700
Ultrasound	$40,000

Other Costs that are to be Capitalized - The Project's other costs to be capitalized include miscellaneous expense associated with the project.

ATTACHMENT 8
Project Status and Completion Schedules

The proposed project plans are still at a schematic stage. The proposed project completion date is July 1, 2026. Financial commitment for the project will occur following permit issuance, but in accordance with HFSRB Regulations.



ATTACHMENT 9
Cost Space Requirements

The equipment will be installed within the existing facility, which encompasses approximately 3,719 gross square feet (GSF). Currently, the Board does not maintain specific space or facility standards for the installation of diagnostic equipment in non-hospital settings, such as a medical office building.

		Gross Square Feet		Amount of Proposed Total Gross Square Feet That Is:			
Dept. / Area	**Cost**	**Existing**	**Proposed**	**New Const.**	**Modernized**	**As Is**	**Vacated Space**
REVIEWABLE							
Diagnostic Radiology	$3,856,364		3,719	3,719			
Total Clinical	$3,856,364		3,719	3,719			
NON-REVIEWABLE							
Administrative	$1,896,842		1,686	1,686			
Total Non-clinical	$1,896,842		1,686	1,686			
TOTAL	**$5,753,206**		**5,405**	**5,405**			

APPEND DOCUMENTATION AS ATTACHMENT 9, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

ATTACHMENT 11
Background of the Applicant

The following information is provided to illustrate the qualifications, background and character of the Applicants.

UroPartners Imaging Center

UroPartners Imaging Center ("UroPartners" or the "Facility") is a dedicated diagnostic facility operated by UroPartners, LLC—one of the largest independent urology group practices in the Midwest. The laboratory was established to meet the highly specialized diagnostic needs of urologic care, supporting the clinical operations of UroPartners' extensive provider network.

Focused exclusively on urologic pathology, the laboratory processes thousands of specimens annually, including prostate biopsies, bladder and kidney tissue, and other genitourinary samples. By centralizing pathology services under one specialized facility, UroPartners ensures diagnostic consistency, clinical accuracy, and expedited turnaround times—key factors in the effective management of urologic malignancies and other complex conditions.

The lab's integration into the broader UroPartners system enables seamless communication between pathologists and urologists, enhancing real-time decision-making and improving overall patient care. Its quality-driven protocols and adherence to best practices in laboratory medicine position it as a critical resource in advancing precision-based urologic treatment. UroPartners intends to acquire major medical equipment for the Facility located at 2225 Enterprise Drive, Suite 3510 Westchester, Illinois 60154.

UroPartners, LLC

UroPartners, LLC is the leading independent urology group in the Midwest, comprising over 90 board-certified urologists, radiation oncologists, pathologists, and advanced practice providers. Structured as a physician-owned and governed corporate entity, UroPartners delivers integrated, specialty-focused care across a wide geographic footprint, with dozens of clinical offices, three dedicated Prostate Centers, surgical affiliations, and an in-house Imaging Center—all serving the greater Chicagoland region and surrounding communities.

Founded with the mission to deliver comprehensive, patient-centered care in all aspects of adult urology, UroPartners offers expertise in general urology, men's health, urologic oncology, kidney stone management, female pelvic health, and advanced minimally invasive surgery. The group's multidisciplinary structure allows for seamless coordination across diagnostics, medical management, surgical intervention, radiation therapy, and ongoing surveillance.

A cornerstone of UroPartners' integrated model is its College of American Pathologists (CAP)-accredited UroPartners Imaging Center, which is fully staffed with fellowship-trained pathologists and laboratory scientists specializing in genitourinary disease. This high-volume diagnostic lab provides rapid and precise results for prostate biopsies, bladder and kidney tissue, cytology, FISH studies, microbiology, and bloodwork. The lab's close integration with UroPartners' clinical and surgical teams fosters real-time collaboration, allowing for faster diagnoses, personalized treatment planning, and improved continuity of care. The ability to conduct and interpret highly specialized pathology work in-house is a significant differentiator that elevates the standard of care and enhances patient outcomes.

The group also maintains and operates three Prostate Centers of Excellence, where patients receive comprehensive diagnostic evaluations, including MRI/ultrasound fusion biopsies, consultations with radiation oncologists, and access to advanced treatment modalities such as brachytherapy, external beam radiation therapy, and active surveillance protocols. These centers represent UroPartners' commitment to innovation and leadership in prostate cancer care.

ATTACHMENT 11
Background of the Applicant

UroPartners is also a leading provider of outpatient urologic procedures, which are performed in its clinics, surgery centers, or affiliated hospitals. The scope of outpatient services includes, but is not limited to:

- Cystourethroscopy
- Stent placements and removals
- Laser fulguration of bladder tumors or lesions
- Lithotripsy for kidney stones
- Circumcision and revision circumcision
- Vasectomy and vasectomy reversal
- MRI/ultrasound fusion-guided prostate biopsies
- Laser vaporization of the prostate (e.g., GreenLight, HoLEP)
- Placement of penile prosthetics
- Excision of hydroceles and varicoceles
- Brachytherapy for prostate cancer

These procedures are supported by state-of-the-art equipment and highly trained staff in both ambulatory surgical settings and physician offices.

In addition to delivering exemplary clinical care, UroPartners plays a vital role in regional education and research initiatives. Many of its physicians hold academic appointments and participate in clinical trials, contributing to the advancement of urologic science and innovation. The group's collaborative approach ensures that every patient receives personalized, evidence-based care tailored to their diagnosis and treatment goals.

Through its integrated model of care, in-house diagnostic capabilities, and subspecialty expertise, UroPartners continues to be a model of excellence in outpatient urology and a trusted provider for thousands of patients across the Midwest.

Solaris Health

Solaris Health is a leading national healthcare platform committed to enhancing access to specialty healthcare and continually improving patient outcomes. Empowering community providers allows Solaris to make sure that every decision puts patient care at the forefront. Solaris has been growing to meet the changing needs of the healthcare providers, and to develop innovative ways to better deliver value and state-of-the-art care to our patients. With 500+ providers treating more than 744,000 unique patients annually, Solaris Health is proud to be among the most innovative medical organizations in the United States. Solaris Health is the management company for the licensee.

ATTACHMENT 11
Background of the Applicant

June 2, 2025

John P. Kniery
Board Administrator
Illinois Health Facilities and Services Review Board
525 W Jefferson Street, Floor 2
Springfield, IL 62761

Re: UroPartners Pathology Lab, Certification and Authorization Letter

Dear Mr. Kniery,

As a representative of Solaris Health Holdings, LLC, I, Gary Kirsh, MD, give authorization to the Health Facilities and Services Review Board and the Illinois Department of Public Health ("IDPH") to access documents necessary to verify the information submitted including, but not limited to: official records of IDPH or other state agencies, the licensing or certification records of other states, and the records of nationally recognized accreditation organizations.

I further verify that Solaris Health Holdings, LLC, has an ownership interest in any other healthcare facility in Illinois, and therefore has had no adverse actions to report for the past three (3) years.

I hereby certify this is true and based upon my personal knowledge under penalty of perjury and in accordance with 735 ILCS 5/1-109.

Sincerely,

Gary Kirsh, M.D.,
Chief Executive Officer
Solaris Health Holdings, LLC

ATTACHMENT 11
Background of the Applicant

June 2, 2025

John P. Kniery
Board Administrator
Illinois Health Facilities and Services Review Board
525 W Jefferson Street, Floor 2
Springfield, IL 62761

Re: UroPartners Pathology Lab, Certification and Authorization Letter

Dear Mr. Kniery,

As a representative of UroPartners, LLC, I, Daniel Scharff, give authorization to the Health Facilities and Services Review Board and the Illinois Department of Public Health ("IDPH") to access documents necessary to verify the information submitted including, but not limited to: official records of IDPH or other state agencies, the licensing or certification records of other states, and the records of nationally recognized accreditation organizations.

I further verify that UroPartners, LLC, has an ownership interest in one other healthcare facility, the UroPartners Surgery Center, LLC. This ambulatory surgical treatment center has had no adverse actions to report for the past three (3) years.

I hereby certify this is true and based upon my personal knowledge under penalty of perjury and in accordance with 735 ILCS 5/1-109.

Sincerely,

Daniel Scharff
Secretary
UroPartners, LLC

ATTACHMENT 12
Purpose of the Project

This project involves the acquisition and installation of three major pieces of medical imaging equipment—a Biograph mCT PET-CT scanner, a mobile Cone Beam CT 3D imaging Cios Spin system with the Artis Q imaging platform, and an Acuson Maple Ultrasound System—at the UroPartners Imaging Center located in Westchester, Illinois. The facility serves patients throughout northern Cook County, DuPage County, and southern Lake County.

Each piece of equipment provides unique and clinically significant benefits that support improved patient care:

- **Biograph mCT PET-CT Scanner:** This hybrid imaging system combines functional positron emission tomography (PET) imaging with high-resolution computed tomography (CT). It is especially beneficial for detecting and staging prostate cancer, assessing treatment response, and identifying recurrence. Integrating PET-CT within the practice allows for faster diagnosis and more accurate treatment planning, reducing delays and unnecessary procedures.

- **Cios Spin Mobile Cone Beam CT with Artis Q Imaging System:** This advanced intraoperative imaging tool allows for real-time, high-resolution 3D imaging during minimally invasive procedures. It supports image-guided interventions, particularly for prostate and renal procedures, by improving precision and reducing the risk of complications. Its mobility ensures flexibility in workflow and enhances safety by reducing the need to transfer patients for separate imaging sessions.

- **Acuson Maple Ultrasound System:** This next-generation ultrasound device offers high-resolution, real-time imaging for soft tissue evaluation and biopsy guidance. It is crucial in the early detection and monitoring of prostate abnormalities, including targeted fusion biopsies. Its superior imaging quality aids in diagnostic accuracy, enabling more personalized and effective patient management.

We have enclosed materials from the manufacturer regarding this critical equipment.

Consistent with the goals and mission of the Health Facilities and Services Review Board, the applicants have filed this application in advance of their existing machine being rendered unusable. The acquisition of a new PET/CT and ultrasound machines will serve the dual purpose of ensuring that the thousands of patients served by UroPartners will continue to have access to life saving treatments offered by the practice. Additionally, the acquisition of new imaging equipment at this time promotes efficient health planning and allows the UroPartners practice to gradually phase out their existing machine while bringing the new cutting-edge machines up to full utilization.

This project proposes to address the regular deterioration of existing equipment and allow the patients served by the largest urology practice in the Midwest to continue to benefit from the care available in response to the acquisition of new state-of-the-art PET/CT and ultrasound equipment. This will allow the practice to continue performing lifesaving procedures for their patients suffering from prostate cancer and other urological conditions.

Prostate Cancer is the most common non-skin cancer in the United States. The Prostate Cancer Foundation reports that 1 out of every 9 men will be diagnosed with prostate cancer in their lifetime. Typically, men at age 50 begin receive routine screening for prostate cancer. If test results reveal an enlargement or irregularity, physicians perform additional tests to determine if the patient in fact suffers from prostate cancer. According to the Illinois Department of Public Health, African Americans and Latinos account for almost 60% of patient deaths due to prostate cancer.

Furthermore, this project will expand access to advanced diagnostic and therapeutic services within the Interventional Radiology and Prostate-Specific Membrane Antigen/ Positron Emission Tomography ("PSMA/PET") service lines.

ATTACHMENT 12
Purpose of the Project

Uterine Fibroid Embolization (UFE)

Uterine fibroids, or leiomyomas, are benign smooth muscle tumors of the uterus that affect a significant proportion of women during their reproductive years. Estimates suggest that by age 50, up to 70% of white women and 80% of African American women will have developed fibroids. In Illinois, particularly in urban centers like Chicago, studies have indicated a higher prevalence of uterine fibroids among African American women, correlating with increased symptom severity and earlier onset.

UFE is a minimally invasive procedure that offers an alternative to surgical interventions such as hysterectomy or myomectomy. The procedure involves the injection of embolic agents into the uterine arteries to block blood flow to fibroids, causing them to shrink and symptoms to subside. Clinical outcomes have demonstrated that UFE effectively reduces symptoms like heavy menstrual bleeding, pelvic pain, and pressure, with a shorter recovery time compared to surgical options.

The integration of advanced imaging technologies, such as the Cios Spin mobile Cone Beam CT system, enhances the precision and safety of UFE procedures. Real-time, high-resolution imaging allows for accurate catheter placement and embolic agent delivery, minimizing risks and improving patient outcomes. This technological advancement is particularly beneficial in outpatient settings, facilitating same-day procedures and reducing hospital stays.

By offering UFE services equipped with cutting-edge imaging, UroPartners addresses a critical need for accessible, uterus-preserving treatment options for women suffering from symptomatic fibroids in Illinois. This approach aligns with broader public health goals of reducing healthcare disparities and improving women's health outcomes.

Ureteral Stent Removal

Ureteral stents are commonly used in urological practice to ensure urine flow from the kidneys to the bladder, particularly after surgeries or in cases of obstruction. Timely removal of these stents is crucial to prevent complications such as infections, encrustation, and discomfort. Studies have shown that protocols emphasizing early stent removal can reduce the incidence of urinary tract infections and other complications without increasing risks.

In Illinois, the demand for efficient stent management is significant, given the prevalence of urological procedures requiring stent placement. The availability of advanced imaging systems, like the Cios Spin, facilitates precise visualization during stent removal, enhancing procedural safety and patient comfort. This is particularly important for female patients, who may experience higher rates of stent-related discomfort and complications.

Implementing streamlined stent removal protocols supported by advanced imaging can lead to improved patient experiences, reduced healthcare costs, and decreased burden on healthcare facilities. By minimizing the risks associated with prolonged stent indwelling times, healthcare providers can enhance overall urological care quality.

UroPartners' initiative to incorporate state-of-the-art imaging technologies for stent management underscores its commitment to delivering high-quality, patient-centered urological care in Illinois. This approach ensures that patients receive timely and effective interventions, reducing the likelihood of complications and improving health outcomes.

ATTACHMENT 12
Purpose of the Project

Kidney Imaging for Clear Cell Renal Cell Carcinoma (ccRCC)

Clear cell renal cell carcinoma (ccRCC) is the most common subtype of kidney cancer, accounting for approximately 75% of cases. In Illinois, kidney cancer represents a significant health concern, with the Illinois State Cancer Registry reporting 2,786 new cases of kidney and renal pelvic cancer in 2021. Of these, 1,028 cases were in women, highlighting the importance of effective diagnostic tools for female patients.

Early and accurate diagnosis of ccRCC is critical for effective treatment planning and improving patient survival rates. Traditional imaging modalities may have limitations in distinguishing ccRCC from other renal masses. The advent of advanced imaging agents, such as Zircaix, offers enhanced specificity for ccRCC detection. Pending FDA approval, this imaging agent will enable non-invasive, accurate identification of ccRCC, facilitating timely and appropriate therapeutic interventions.

The integration of PET/CT imaging with novel agents like Zircaix into clinical practice represents a significant advancement in renal oncology. This technology provides clinicians with detailed insights into tumor biology, aiding in the differentiation of malignant and benign lesions, and informing decisions regarding surgery, systemic therapy, or active surveillance.

By adopting these cutting-edge imaging modalities, UroPartners positions itself at the forefront of renal cancer diagnostics in Illinois. This commitment to innovation ensures that patients have access to the most accurate and effective diagnostic tools, ultimately leading to improved treatment outcomes and survival rates for those affected by ccRCC.

The acquisition of this equipment aligns with UroPartners' commitment to delivering advanced, patient-centered care in an efficient outpatient environment. As described in this application, the applicants have an ample patient population that will benefit from this new equipment. By offering comprehensive diagnostic imaging services onsite, the center can reduce reliance on hospital-based imaging, lower overall healthcare costs, and improve patient access to timely, high-quality care. The strategic investment also addresses regional needs by expanding access to advanced imaging technologies for patients in northern Cook, DuPage, and southern Lake Counties—areas with a growing demand for specialized urologic care.

All-in-all, this project enhances the capability of UroPartners to provide leading-edge, efficient, and accurate diagnostic and treatment services, ultimately improving outcomes and patient satisfaction across the communities it serves.

References:

1. Ndebele S, Turner T, Liao C, et al. Uterine Fibroid Prevalence in a Predominantly Black, Chicago-Based Cohort. *Int J Environ Res Public Health*. 2023;20(1):123. PubMed+3ResearchGate+3ResearchGate+3
2. Evaluation of a Ureteral Stent Removal Protocol in Adult Kidney Transplant Recipients. *Open Forum Infect Dis*. 2024;11(9):ofae510. PMC+2Oxford Academic+2ResearchGate+2
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4. Telix Pharmaceuticals. FDA Accepts BLA for TLX250-CDx (Zircaix®) for Kidney Cancer Imaging, Grants Priority Review. https://telixpharma.com/news-views/fda-accepts-bla-for-tlx250-cdx-zircaix-for-kidney-cancer-imaging-grants-priority-review/
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ATTACHMENT 12
Purpose of the Project

Biograph mCT PET-CT Scanner

PET technology that takes you further

Our foundation of reliable, sustainable, and proven technologies allows you to start from a position of clinical power. Biograph mCT streamlines the user experience and addresses a broader patient population with a design purposefully built on our key technology. Evolve your business with a scalable PET/CT platform that opens new opportunities and helps maximize and protect your investment for the future.

Experience more PET technologies[1]

TrueV
Extend the PET axial field of view from 16.4 to 22.1 cm and add 33% more detector elements, resulting in 70% higher count rate performance[4].

ultraHD-PET
Improve image signal-to-noise by utilizing TOF combined with the resolution recovery of HD-PET. Enhance image quality and/or reduce patient acquisition time.

FlowMotion/FlowMotion AI
Create standardized imaging workflows for fast, reproducible, and personalized results with disease-based protocols that adjust to the patient's anatomy.

Whole-body dynamic imaging
Simplify workflow for whole-body dynamic imaging that potentially enables new clinical PET applications.

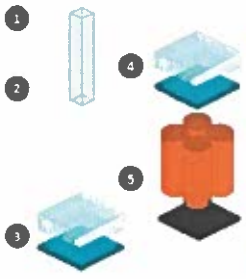
Multiparametric PET AI
Expand the available parameters and acquisition flexibility, facilitate more reproducible images, and enable absolute quantification.

OncoFreeze™ AI
Locate and correct anatomy impacted by respiratory motion and increase clinical confidence without additional setup or patient interaction.

Cardiac imaging
Complete myocardial blood flow (MBF) workflow with automated PET and CT data registration, and fast reconstruction of dynamic datasets simultaneously with acquisition.

QualityGuard™
Use intrinsic radioactive properties of LSO to automatically calibrate the scanner—eliminating the need for an external source for daily and weekly PET quality control and saving technologist time.

Biograph mCT's high 78-mm³ volumetric resolution[2] and small, 4 x 4-mm lutetium oxyorthosilicate (LSO) crystal elements bring enhanced detectability with accurate and reproducible quantification. True time-of-flight (TOF) capabilities and innovative technologies such as FlowMotion™ help you lead the way in technological and medical advancement. Powerful CT solutions ranging from 40 to 128 slices with low-dose technologies give you the flexibility to go beyond standard care.



1 A fast, efficient scintillator, LSO is grown and cut in-house through a vertically integrated manufacturing process, ensuring the highest quality

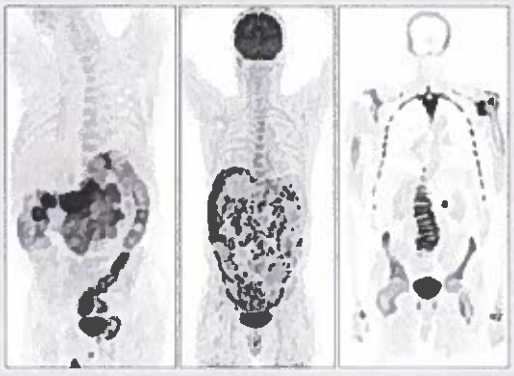
2 4 x 4 x 20-mm crystal elements are individually selected and deliver high 78-mm³ isotropic volumetric resolution; higher image resolution may result in improved lesion detectability

3 Small, 4 x 4-mm crystals with integrated light guidance arranged in a 13 x 13 matrix create a block that is combined with a light guide without partitions to spread light to photomultiplier tube (PMT) photosensors

4 Digital LSO-based detectors and high-speed electronics support true TOF for improved signal-to-noise ratio. This enables faster scans, lower injected dose, and better image quality

5 Arranged with no gaps between detector blocks, the detector delivers an effective sensitivity of up to 23.1 cps/kBq[2] and an effective peak NEC rate of up to 425 kcps[3]

Achieve excellent image quality with combined HD-PET and TOF

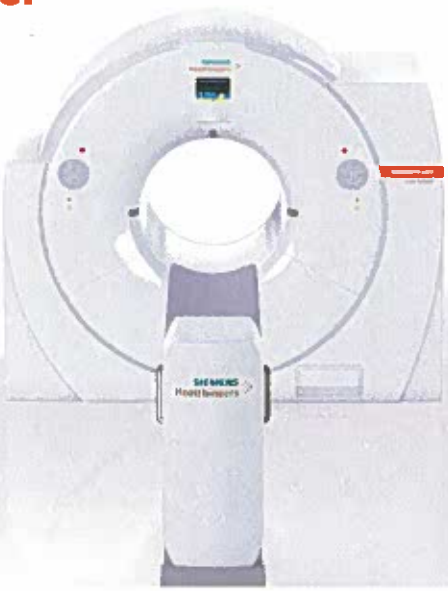


Sarcoma of the mesentery | Peritoneal metastases | Degenerative changes

ATTACHMENT 12
Purpose of the Project

CT technology that takes you further

Biograph mCT is engineered as a true dual-modality scanner, which integrates the best performance of both PET and CT into a single compact system. Available in CT configurations of up to 128 acquired slices per rotation, it provides all the functionalities of high-end standalone CT, including intervention, so that it can potentially generate revenue by performing dedicated CT scans. Requiring just one room and one team, it saves you space, time, and cost.



49%

of Biograph mCT users perform standalone CT examinations in addition to PET/CT scans[2].

Experience more CT technologies[3]

6/-/64-/128-slice CT
Definition class CT offers acquired 40-, 64-, or 128-Edge-slice CT configurations.

SAFIRE
Enhance patient outcomes by delivering excellent image quality at very low doses.

iMAR
Yield images with a reduced level of metal artifacts compared to conventional reconstruction.

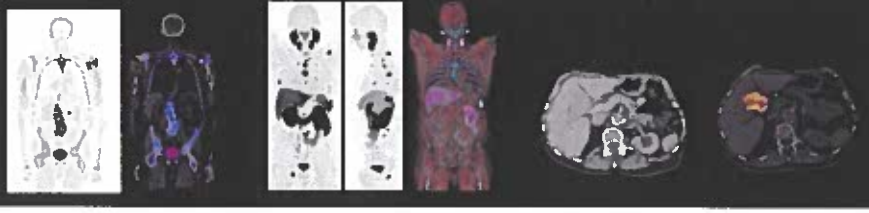
Dual energy
Combine tissue information with morphology using different kV levels.

FAST CARE CT technologies
Optimize dose, image quality and streamline workflow. Innovations include CARE Dose4D™, CARE kV, and more.

Radiation therapy (RT) planning
Support RT workflow, including motion management solutions for precise therapy planning.

Oncology

Expand capabilities beyond traditional PET/CT imaging with Biograph mCT. Designed to support low dose and fast imaging, Biograph mCT enables a comprehensive oncology imaging workflow. Dedicated technologies, such as diaphragm gating, whole-body dynamic imaging, and RT planning packages reveal critical details while ensuring patient comfort.



ATTACHMENT 12
Purpose of the Project

Cios Spin Mobile Cone Beam CT with Artis Q Imaging System

New perspectives.
Full control.

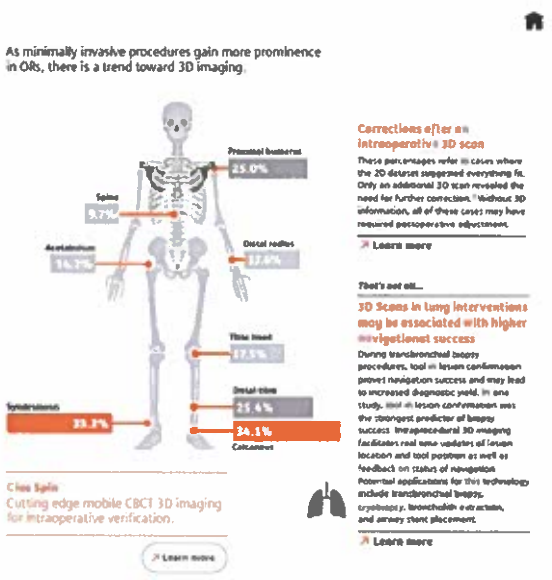
Conventional 2D imaging may not always provide enough information to verify anatomy location and relative placement of screws, implants or tools in demanding procedures.

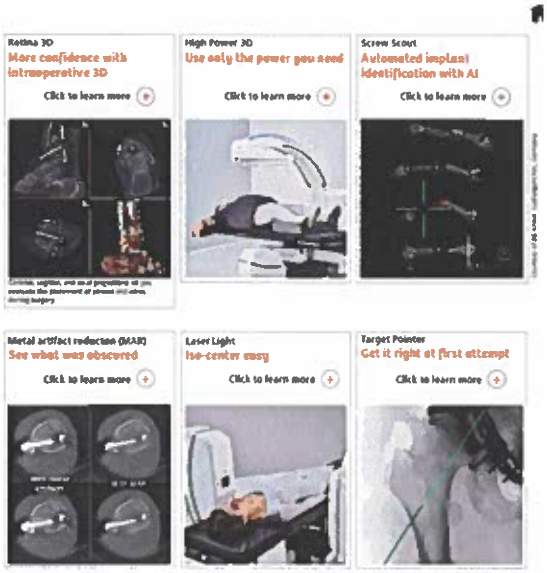
Intraoperative Cone Beam CT (CBCT) 3D imaging can therefore be an important factor in avoiding postoperative complications and improving procedural outcomes.

To provide outstanding 3D capabilities that can be seamlessly integrated into clinical routine, we have developed Cios Spin®: a mobile 2D and CBCT 3D C-arm that delivers precise 3D images for intraoperative verification and peace of mind. You get the best of both worlds: 2D imaging can be used to visualize location of the devices and proper patient anatomy. 3D CBCT can be used to check for integral changes before the procedure and can be used intraoperatively to verify anatomy and relative device placement.

Cios Spin
Cutting-edge mobile CBCT 3D imaging for intraoperative verification.

Learn more





ATTACHMENT 12
Purpose of the Project

Trends in Interventional Radiology

Stroke

Increase of interventional stroke treatment due to superiority of mechanical thrombectomy.

TACE

New and established embolization procedures are on the rise, ranging from, e.g., TACE to PAE.

CLI

Use of endovascular recanalizations to minimize amputations in patients with CLI.

Trends in Surgery

Surgery

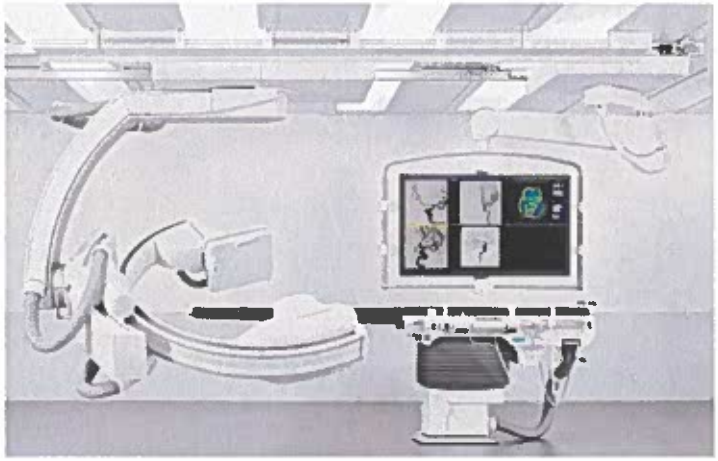
Instead of open surgery, most surgeries will be performed minimally invasively.

3D imaging

3D imaging will become increasingly important to guide surgical procedures.

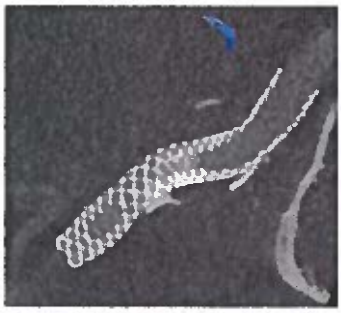
Robotics

3D imaging will also enable robotics to play a larger role in Surgery.



ATTACHMENT 12
Purpose of the Project

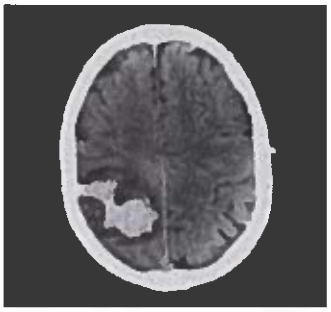
Applications for advanced interventional imaging



University Hospital Erlangen, Germany

Boosting the level of detail
syngo DynaCT Micro

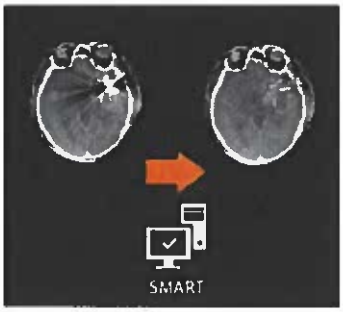
- 40% increased spatial resolution compared to standard *syngo* DynaCT
- Better visualization of finest structures
- Enhanced evaluation of, e.g., stents, flow diverters, or stapes prosthesis



University Hospital Magdeburg, Germany

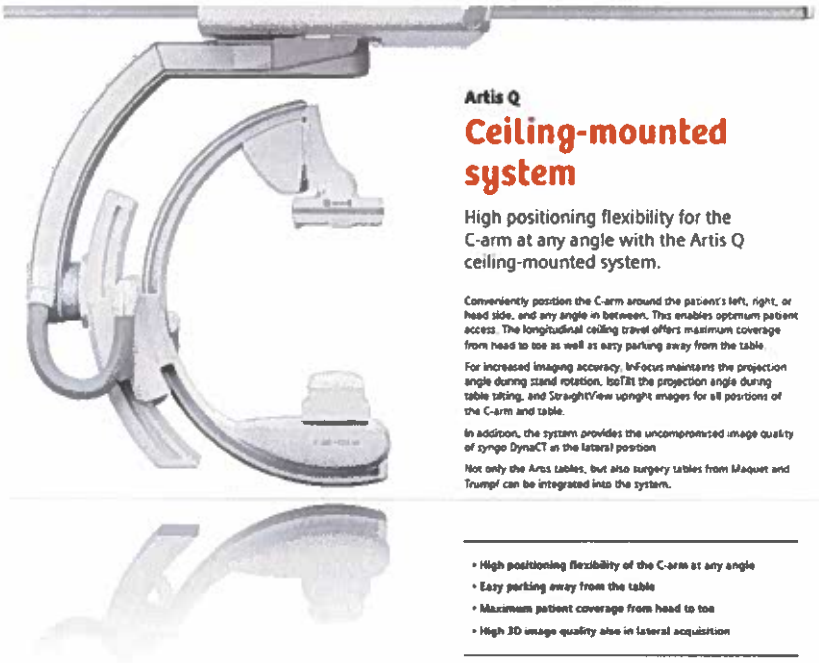
16-bit HDR detector technology
syngo DynaCT

- Homogeneous image representation
- Excellent soft-tissue resolution, also near the skull
- Visualization of bleedings



Reduce metal artifacts to see the unseen
syngo DynaCT SMART

- Reduce artifacts from dense objects using the iterative *syngo* DynaCT SMART volume reconstruction
- Make relevant aspects in soft tissue visible even close to, e.g., coil packages or glue for sounder decision- making during interventions



Artis Q

Ceiling-mounted system

High positioning flexibility for the C-arm at any angle with the Artis Q ceiling-mounted system.

Conveniently position the C-arm around the patient's left, right, or head side, and any angle in between. This enables optimum patient access. The longitudinal ceiling travel offers maximum coverage from head to toe as well as easy parking away from the table.

For increased imaging accuracy, InFocus maintains the projection angle during stand rotation, IsoTilt the projection angle during table tilting, and StraightView upright images for all positions of the C-arm and table.

In addition, the system provides the uncompromised image quality of *syngo* DynaCT in the lateral position.

Not only the Artis tables, but also surgery tables from Maquet and Trumpf can be integrated into the system.

- High positioning flexibility of the C-arm at any angle
- Easy parking away from the table
- Maximum patient coverage from head to toe
- High 3D image quality also in lateral acquisition

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Acuson Maple Ultrasound System:

Designed for versatility

The right tools are essential for a confident examination and diagnosis. ACUSON Maple is a premium, shared-service ultrasound system that provides an enhanced user experience and offers a set of features optimized for the hardworking, everyday needs of all main clinical areas.

ACUSON Maple is designed and built to keep up with the demands of today's clinical realities, with a compact footprint for maneuverability to fit into smaller exam areas

System up/down

Monitor forward

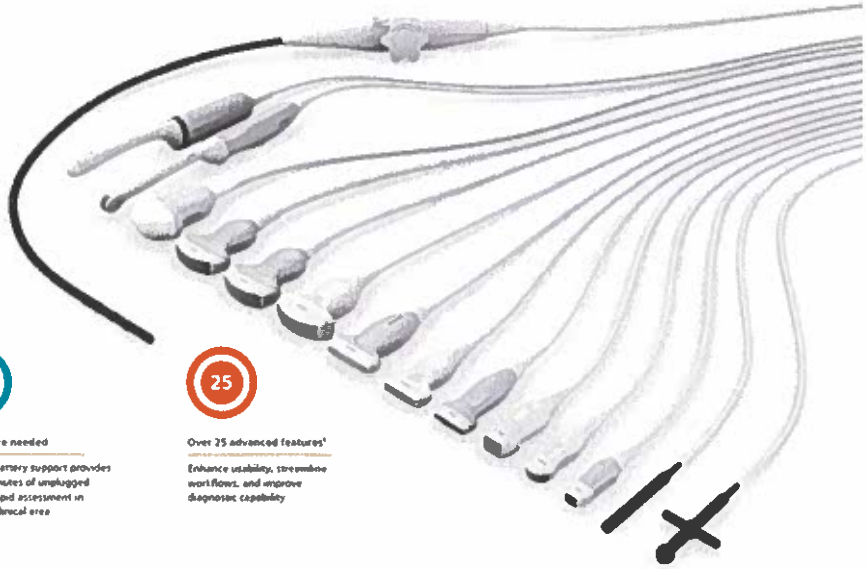
Monitor arm base swivel

80° rotation

80° right/left rotation for user flexibility in choosing transducer connectors position.

Take a closer look at what's possible for every patient, every day

With a large selection of transducers and advanced features that provide more options and capabilities, ACUSON Maple is designed to maximize performance and enable a confident exam across clinical specialties



15

15 transducers

Get the versatility you need to cover a wide range of clinical applications

75

Power where needed

Integrated battery support provides up to 75 minutes of unplugged power for rapid assessment in nearly any clinical area

25

Over 25 advanced features[1]

Enhance usability, streamline workflows, and improve diagnostic capability

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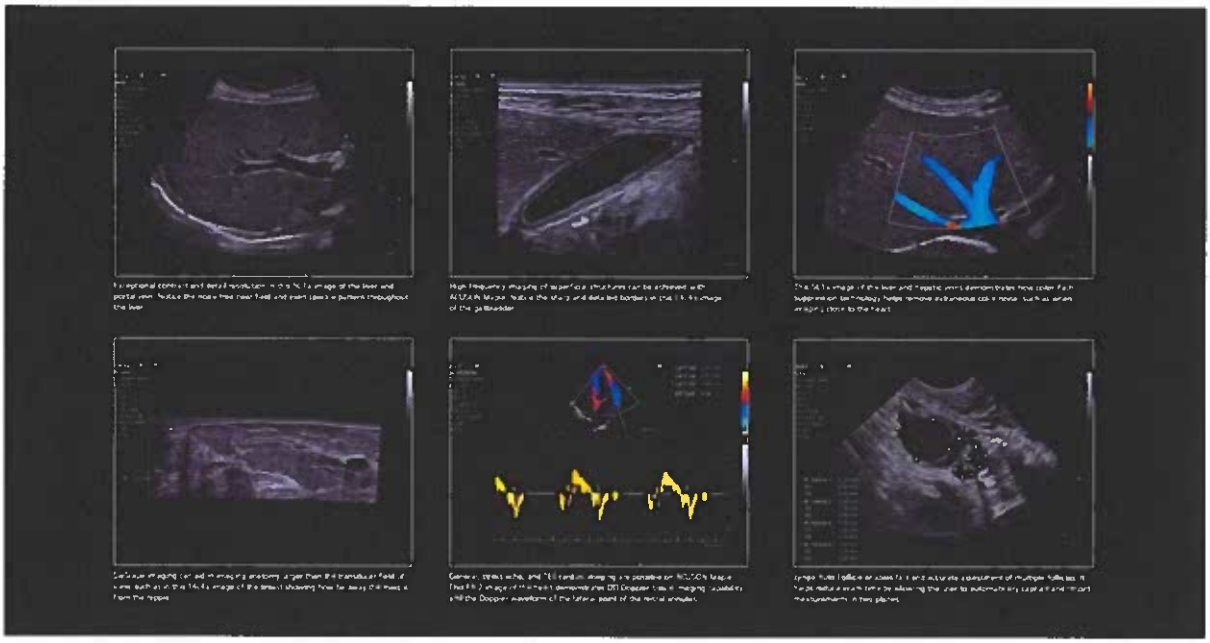

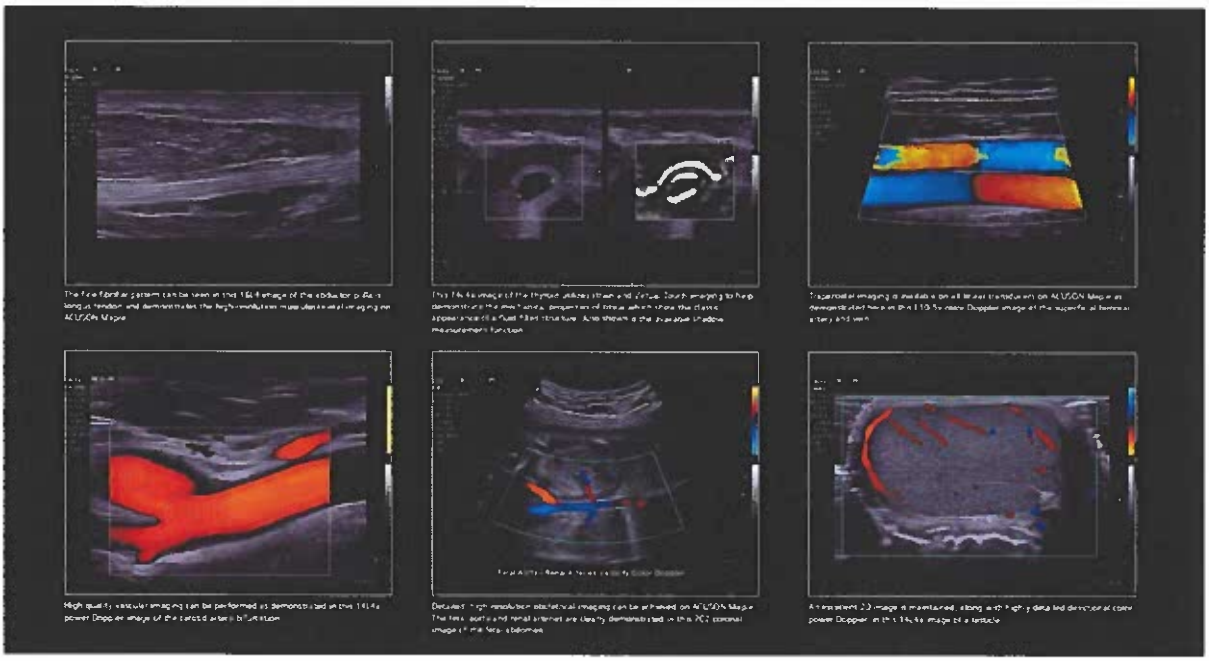

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International Journal of *Environmental Research and Public Health*

MDPI

Article

Uterine Fibroid Prevalence in a Predominantly Black, Chicago-Based Cohort

Sithembinkosi Ndebele [1], Tecora Turner [2], Chuanhong Liao [1], Briseis Aschebrook-Kilfoy [1,3], Nina Randorf [1], Habibul Ahsan [1,3], Kunle Odunsi [4,5] and Obianuju Sandra Madueke-Laveaux [5,*]

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Abstract: (1) Objectives: To investigate the effect of individual-level, neighborhood, and environmental variables on uterine fibroid (UF) prevalence in a Chicago-based cohort. (2) Methods: Data from the Chicago Multiethnic Prevention and Surveillance Study (COMPASS) were analyzed. Individual-level variables were obtained from questionnaires, neighborhood variables from the Chicago Health Atlas, and environmental variables from NASA satellite ambient air exposure levels. The Shapiro–Wilk test, logistic regression models, and Spearman's correlations were used to evaluate the association of variables to UF diagnosis. (3) Results: We analyzed 602 participants (mean age: 50.3 ± 12.3) who responded to a question about UF diagnosis. More Black than White participants had a UF diagnosis (OR, 1.32; 95% CI, 0.62–2.79). We observed non-significant trends between individual-level and neighborhood variables and UF diagnosis. Ambient air pollutants, PM2.5, and DSLPM were protective against UF diagnosis (OR 0.20, CI: 0.04–0.97; OR 0.33, CI: 0.13–0.87). (4) Conclusions: Associations observed within a sample in a specific geographic area may not be generalizable and must be interpreted cautiously.

Keywords: uterine fibroids; leiomyomas; myomas; fibroids; pollution; environmental justice

check for updates

Citation: Ndebele, S.; Turner, T.; Liao, C.; Aschebrook-Kilfoy, B.; Randorf, N.; Ahsan, H.; Odunsi, K.; Madueke-Laveaux, O.S. Uterine Fibroid Prevalence in a Predominantly Black, Chicago-Based Cohort. *Int. J. Environ. Res. Public Health* **2024**, *21*, 222. https://doi.org/10.3390/ijerph21020222

Academic Editors: Eusebio Chiefari and Maria Grazia Porpora

Received: 7 December 2023
Revised: 1 February 2024
Accepted: 12 February 2024
Published: 14 February 2024

1. Introduction

Uterine fibroids (UFs) are the most common benign neoplasm affecting women of reproductive age [1]. They are the leading cause of hysterectomy in the US and worldwide and are a source of significant socioeconomic burdens [1]. Black women are disproportionately affected by UFs, with a higher disease prevalence, earlier onset of disease, and more severe symptoms and disease progression [2]. This disproportionate burden of UFs and other female health conditions is increasingly understood in a framework of health inequity and the social and structural drivers of health [3]. Well-established risk factors that may contribute to the high prevalence of UFs in Black individuals include socioeconomic status, adverse environmental exposures, and experiences that increase chronic stress [4,5]. Each of these factors is believed to converge to increase inflammation within the uterine myometrium, resulting in somatic mutations (such as Med12) that transform normal myometrium stem cells and lead to UF tumor formation [6].

In addition, many lifestyle and socioeconomic factors, such as BMI, alcohol use, income, and occupation, correlate closely with neighborhood characteristics, e.g., access to healthy food and healthcare, exposure to environmental pollutants, and concentrated poverty [5,6]. Neighborhood poverty has been widely studied and is identified as a possible

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determinant of UF prevalence [7,8]. Poor and disenfranchised neighborhoods are often characterized by high crime rates, food insecurity, and other important social determinants of health [9–11]. Lastly, while respiratory and cardiovascular diseases are most often linked to air pollution, recent studies have shown that air pollution is positively associated with the risk of gynecological diseases [12,13], and exposure to air pollutants such as ozone and PM 2.5 may contribute to the racial disparities in UF incidence, prevalence, and severity [14]. The biological mechanism by which air pollutants, e.g., ozone, increase fibroid formation is unclear. Theories such as oxidative stress and immune-inflammatory and hypertension-mediated pathways have been proposed [13].

Cook County, of which 85% is Chicago, has been ranked among the worst 10% of counties in the United States air quality indicators [15]. Therefore, Chicago provides a unique opportunity to examine the potential impact of air pollutants, as well as other urban risk factors, on the prevalence of UFs. Since 2013, a predominantly Black population on Chicago's South Side has been enrolled in the Chicago Multiethnic Prevention and Surveillance Study (COMPASS) with the goal of mitigating health disparities [16]. To this end, extensive data have been collected to understand individual, neighborhood, and environmental factors relevant to disease prevention, disparity mitigation, and improved health outcomes. In this study, we analyzed data from a sample of participants enrolled in this existing longitudinal cohort study to assess the relationship between individual-level, neighborhood, and environmental variables and UF prevalence.

2. Methods

2.1. *Study Design*

This cross-sectional study analyzed the baseline data of a sample of participants from COMPASS. Data included in this study were collected from July 2019–May 2020. A more detailed description of the COMPASS study design can be found elsewhere [16].

2.2. *Study Population*

The sample analyzed in this study was obtained from COMPASS. Established in 2013, COMPASS is a longitudinal prospective cohort study that includes 8000 participants in the City of Chicago. Its purpose is to assess the influence of factors, such as neighborhood, environment, exposure to air pollutants, socioeconomic status, healthcare access, lifestyle, behavior, and genetics, on the health of Chicagoans. COMPASS enrolls residents of the greater Chicago area who are at least 18 years of age and not incarcerated at the time of enrollment. The survey was designed by co-authors Drs. Aschebrook-Kilfoy and Ahsan. Most survey items are harmonized with existing NIH/NCI surveys.

To investigate the possible correlation between these above-mentioned factors and UF diagnosis, we analyzed data of COMPASS participants who responded to the question, "Has a doctor or healthcare professional ever diagnosed you with uterine fibroids?" Based on their responses, we categorized participants into two groups: those who had received a UF diagnosis (yes) and those who had not (no).

2.3. *Individual-Level Variables*

Demographic factors such as age, race, and ethnicity, as well as lifestyle and behavioral factors, including activity levels, alcohol intake, and smoking, were reported through the questionnaire. Additionally, access to healthcare, neighborhood factors, such as crime and safety, socioeconomic status, including employment status and income status, and reproductive history, including pregnancy and hysterectomy, were reported through the questionnaire. All participants in the sample listed female as their gender. We categorized participants as either active or inactive based on their reported participation in at least one of the 15 physical activities listed in the questionnaire (ranging from household chores to vigorous workouts). Participants were classified as "smokers" if they reported smoking cigarettes, cigars, marijuana, or vaping nicotine and/or tobacco daily or weekly. Participants were classified as "alcohol consumers" if they reported regular alcohol consumption

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and the intake of multiple alcoholic beverages within the last 12 months. Employment status was divided into four categories: employed, unemployed, retired, or unknown. Income status was divided into three categories: low income (USD 34,999 or less), middle income (USD 35,000–USD 89,999), and high income (USD 90,000 or above).

Access to healthcare was assessed using two variables: "access to care" and "quality of care". The metric for access to care was determined by combining participants' responses to questions on where they go for health care (i.e., urgent care, emergency room, clinic visit, etc.), their perception of the number of doctors in their community, and whether they had ever been turned away by a doctor for financial or insurance reasons. Quality of care was evaluated based on participants' satisfaction with the care they received in the last 12 months and their agreement with statements about their doctors' medical knowledge and the amount of time spent with patients.

2.4. Neighborhood Variables

To investigate the possible impacts of participants' perception of neighborhood crime and violence on physical activity levels, participants' responses to questions regarding their choice to forego exercise due to concerns about crime and violence, as well as the impact of these concerns on their daily lives, were assessed. Contextual neighborhood variables were analyzed using Chicago Health Atlas (CHA) data for each Chicago community area between 2015 and 2019 [17]. Chicago has distinct community areas (aka neighborhoods). COMPASS links survey data to community areas, and CHA data are merged into COMPASS data on the shared community area level. Six neighborhood variables were included: the hardship index (composite score reflecting hardship in the community), the neighborhood safety rate (% of adults who report that they feel safe in their neighborhood "all the time" or "most of the time"), low food access (% of residents who must travel further than ½ mile to the nearest supermarket in urban areas or 10 miles in rural areas), traffic intensity (proximity to vehicle traffic), the social vulnerability index (percentile relative vulnerability based on social factors), and the rate of received needed care (% of adults who report that it is "usually" or "always" easy to obtain care with their health plan).

2.5. Environmental Variables

Ambient exposure data, including PM2.5, ozone, diesel particulate matter (DSLPM), and proximity to traffic (PTRAF), was extracted from COMPASS, which obtains air quality data by geocoding participant-supplied addresses and linking them to one of 77 Chicago community areas and their census tract or block. These ambient exposure levels are derived from the 2019 Environmental Justice Screening (EJSCREEN) air quality data and merged with the COMPASS data set using the EJSCREEN ID variable at the census Federal Information Processing Standards (FIPS) code block group level.

2.6. Statistical Analysis

Descriptive statistics of the investigated variables from the COMPASS dataset and the selected contextual neighborhood variables retrieved from the Chicago Health Atlas (CHA) for each Chicago community were linked to individual participants. The mean ± standard deviation (SD) or median [interquartile range (IQR)] was reported for continuous variables based on data normal distribution, and frequencies and percentages were presented for categorical variables. The Shapiro–Wilk normality test was used to examine whether the variables were normally distributed. Differences in subject characteristics between groups were analyzed by two-sample t-tests or Mann–Whitney tests, depending on the distributions for continuous variables, and by Pearson's chi-squared or Fisher's exact test for categorical variables. Logistic regression was used to investigate trends in age, race, access to quality care, behavioral lifestyle, contextual neighborhood factors, socioeconomic status, and ambient exposures related to UF, illustrating the odds ratio (OR) value with a 95% confidence interval (CI). In addition, potential risk factors for UFs were identified in the multivariable logistic regression model. Of note, a multilevel model was not uti-

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lized to analyze the contextual neighborhood variables because the available data had no hierarchical or clustered structure. We used Spearman's rank correlation coefficient with Bonferroni correction to assess the contextual neighborhood correlations because the contextual neighborhood data did not have approximately normal distributions. Mixed positive and negative correlations did not satisfy the critical assumption of unidirectionality needed for the weighted quantile sum (WQS) analysis for the overall mixture effect of neighborhood characteristics, which was performed in a similar study by a co-author, Dr Aschebrook-Kilfoy [18,19]. Lastly, multivariable logistic regression was performed to assess the impact of contextual neighborhood variables on UF diagnosis adjusted by race and household income status. Two-sided $p < 0.05$ was considered statistically significant. All the analyses were conducted using Stata/SE software 17.0 (StataCorp LLC, College Station, TX, USA).

3. Results

A total of 602 participants aged 35–76 years (mean (SD): 50.3 ± 12.3) met the criteria for this study, and 21% self-reported a UF diagnosis. See Table 1 for a summary of participants' demographics, lifestyle, and reproductive history. Univariate analysis of each variable is reported in this section unless otherwise indicated.

Table 1. Summary of Participants' demographics, lifestyle, and reproductive history.

	Entire Sample (n = 602)	Fibroid Diagnosis (n = 127)	No Fibroid Diagnosis (n = 475)	*p*-Value
Age (year), mean ± SD	50.3 ± 12.3	37.1 ± 10.5	53.8 ± 10.1	<0.001
BMI, mean ± SD	31.4 ± 9.0	32.2 ± 7.8	31.2 ± 9.3	0.265
Race, n (%)				
Black	513 (85.2)	111 (87.4)	402 (84.6)	0.792
White	52 (8.6)	9 (7.1)	43 (9.1)	
Other	37 (6.2)	7 (5.5)	30 (6.3)	
Ethnicity, n (%)				
Non-Hispanic	546 (90.7)	113 (89.0)	433 (91.2)	0.391
Hispanic	10 (1.7)	1 (0.8)	9 (1.9)	
Unknown	46 (7.6)	13 (10.2)	33 (7.0)	
Socioeconomic Status, n (%)				
Employment Status				
Employment	127 (21.1)	30 (23.6)	97 (20.4)	0.360
Unemployed	368 (61.1)	72 (56.7)	296 (62.3)	
Retired	65 (10.8)	18 (14.2)	47 (9.9)	
Unknown	42 (7.0)	7 (5.5)	35 (7.4)	
Income Status [a]				
Low income	422 (70.1)	83 (65.4)	339 (71.4)	0.337
Middle income	44 (7.3)	8 (6.3)	36 (7.6)	
High Income	31 (5.2)	9 (7.1)	22 (4.6)	
Unknown	105 (17.4)	27 (21.3)	78 (16.4)	

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Table 1. *Cont.*

	Entire Sample (n = 602)	Fibroid Diagnosis (n = 127)	No Fibroid Diagnosis (n = 475)	*p*-Value
Behavioral Lifestyle, n (%)				
Alcohol/Smoking Status				
Smoking Status				
Smoker	312 (51.8)	72 (56.7)	240 (50.5)	0.231
Non-Smoker	290 (48.2)	55 (43.3)	235 (49.5)	
Alcohol Consumption				
Consumer	105 (17.4)	29 (22.8)	76 (16.0)	0.623
Non-Consumer	243 (40.4)	61 (48.0)	182 (38.3)	
Unknown	254 (42.2)	37 (29.1)	217 (46.7)	
Reproductive History, n (%)				
Pregnancy outcome				
Live birth	375 (62.3)	79 (62.2)	296 (62.3)	0.385
Pregnancy loss	51 (8.47)	14 (11)	37 (7.8)	
Abortion	62 (10.3)	15 (11.8)	47 (9.9)	
Not reported	114 (18.9)	19 (15)	95 (20)	
Hysterectomy	97 (16.4)	57 (45.6)	40 (8.6)	<0.001

Income Status [a]: Income status ranges. Low income: USD 34,999 or less. Middle income: USD 35,000–USD 89,999. High income: USD 90,000 or above.

3.1. Individual-Level Variables

3.1.1. Demographic Factors

The average age of participants with a UF diagnosis was 37 years. In our sample, 85% identified as Black, 9% as White, and 6% as other. The odds of a UF diagnosis decreased with age (OR, 0.85; 95% CI, 0.83 to 0.88). Black participants had higher odds of a UF diagnosis when compared to White participants (OR, 1.32; 95% CI, 0.62 to 2.79) or others (OR, 1.11; 95% CI, 0.37 to 3.32). A total of 90.7% of the sample were non-Hispanic, 7.6% were unknown, and 1.7% were Hispanic. Participants of Hispanic ethnicity had lower odds of a UF diagnosis (OR, 0.43; 95% CI, 0.05 to 3.40). The mean age of participants with a UF diagnosis was lower in Black (36.5 years) compared to White (41.6 years) or participants of other races (41 years), with a *p*-value of 0.330 (Figure 1A).

3.1.2. Socioeconomic Factors

Seventy percent of the participants were in the low-income bracket. Those in higher income brackets had increased odds of a UF diagnosis. Unemployed participants had decreased odds of a UF diagnosis (OR, 0.79; 95% CI, 0.48 to 1.28), and 39% of the sample participants reported having no access to quality healthcare. Patients with access to quality care were approximately 26% less likely to receive a UF diagnosis (OR, 0.74; 95% CI, 0.50 to 1.09). A total of 42% of the sample participants reported having an insufficient number of doctors in their community. Participants who reported having enough doctors in their community had lower odds of a UF diagnosis (OR, 0.96; 95% CI, 0.61 to 1.52). A total of 42% of participants reported concerns about crime and neighborhood violence. Participants who had daily concerns about crime trended towards higher odds of receiving a UF diagnosis (OR, 1.19; 95% CI, 0.79 to 1.79) compared to those who did not have these concerns (Figure 1B).

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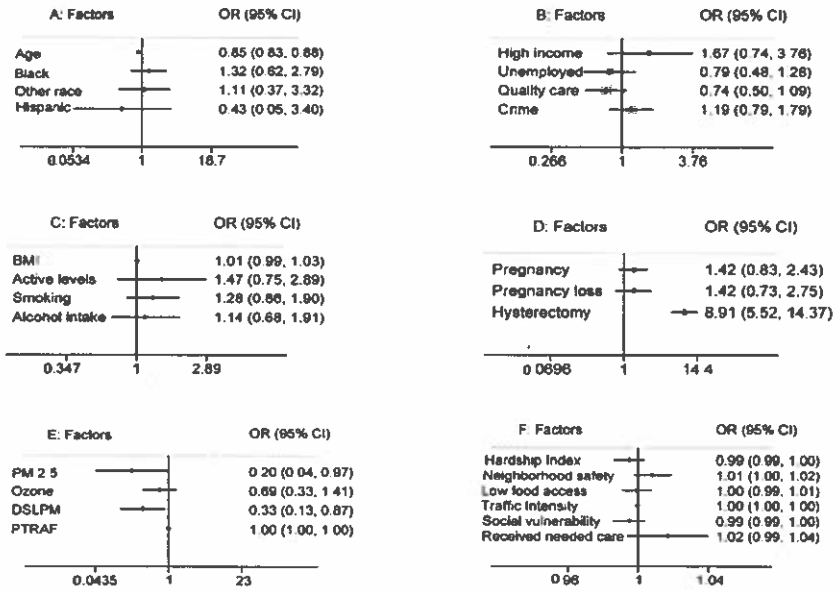

Figure 1. (A) Odds of UF diagnosis by Demographic factors: Age, Race (Black), ethnicity. Odds ratio and 95% Confidence Interval (CI) were utilized for an interquartile range where continuous predictors of age compared quartile 3 with quartile 1. Categorical predictors of Race, Daily Exercise, and Active Lifestyle utilized simple odds and compared them to a reference group (White, normal BMI, No exercise, not active lifestyle). Odd ratios above 1 indicate an increased risk of developing uterine fibroid. Age: continuous variable. Race: White, Black, and Other. **(B) Odds of UF diagnosis by Income/Employment Status, Access to Quality Care, and Crime.** Categorical predictors of Income status, Employment status, access to quality care, and crime utilized simple odds and compared them to a reference group (low income, employed, no quality care, not enough doctors, and no crime). Odd ratios above 1 indicate an increased risk of developing uterine fibroid. Conversely, an odds ratio of less than 1 represents a protective effect. **(C) Odds of UF diagnosis by lifestyle and behavioral: BMI, activity levels, alcohol intake, smoking.** Odds ratio and 95% Confidence Interval (CI) were utilized for an Interquartile range where continuous predictor BMI compared quartile 3 with quartile 1. Categorical predictors of smoking status, secondhand smoking exposure, and alcohol consumption utilized simple odds and compared them to a reference group (normal BMI, No exercise, not active lifestyle, no alcohol intake, and no smoking). Odd ratios above 1 indicate an increased risk of uterine fibroid diagnosis. BMI: Underweight, Normal, Overweight, Obese. Daily exercise: No exercise, daily exercise. Active lifestyle: Inactive lifestyle, active lifestyle. **(D) Odds of UF diagnosis by pregnancy and hysterectomy history.** Categorical predictors' previous pregnancy status, Pregnancy loss experience, and hysterectomy utilized simple odds and compared them to a reference group of zero or not experienced. Odd ratios above 1 indicate an increased odds of uterine fibroid diagnosis. **(E) Odds of UF diagnosis by Ambient Exposure Ranges.** Odd ratios above 1 indicate an increased risk of developing uterine fibroid. Conversely, an odds ratio of less than 1 represents a protective effect. **(F) Odds of UF diagnosis by Neighborhood contextual variables.** Odd ratios above 1 indicate an increased risk of developing uterine fibroid. Conversely, an odds ratio of less than 1 represents a protective effect.

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3.1.3. Lifestyle and Behavioral Factors

Fifty-two percent of participants were categorized as obese (BMI > 30), 24% as overweight (BMI 25 to <30), 20% as healthy weight (BMI 18.5 to <25), and 4% as underweight (BMI < 18.5). We observed a positive trend between BMI and a UF diagnosis; obese participants had 1.5 times higher odds of a UF diagnosis compared to participants with a normal BMI (OR, 1.49; 95% CI, 0.87 to 2.56). UF diagnoses were less likely in participants who reported daily exercise (OR, 0.93; 95% CI, 0.59 to 1.48). Within our sample, 88.5% of the participants reported having an active lifestyle, and these participants were more likely to have a UF diagnosis (OR, 1.47; 95% CI, 0.75 to 2.89). Fifty-two percent of the sample participants were smokers, and they were 1.28 times more likely to have a UF diagnosis (OR, 1.28; 95% CI, 0.86 to 1.90). Additionally, 44% of the sample participants reported childhood secondhand smoke exposure, which was associated with increased odds of a UF diagnosis (OR, 1.46; 95% CI, 0.84 to 2.52). Of the sample participants, 17% reported regular alcohol consumption (every day or every week), 40% denied regular alcohol use, and 42% reported unknown alcohol usage. Those who reported regular alcohol use were 1.14 times more likely to have a UF diagnosis (OR, 1.14; 95% CI, 0.68 to 1.91) (Figure 1C).

3.1.4. Reproductive History

A history of pregnancy was reported by 81% of participants. These participants had higher odds of a UF diagnosis (OR, 1.42; 95% CI, 0.83 to 2.43). The odds of a UF diagnosis were also higher in participants who experienced pregnancy loss (OR, 1.42; 95% CI, 0.73 to 2.75). Abortions were slightly more common among participants with a UF diagnosis (OR, 1.19; 95% CI, 0.43 to 1.30). Sixteen percent of participants reported having a hysterectomy, while 84% denied having undergone the procedure. The odds of a UF diagnosis were 8.9 times higher in participants who had undergone a hysterectomy (OR, 8.91; 95% CI, 5.52 to 14.37) (Figure 1D).

3.2. Neighborhood Variables

Except for traffic intensity, neighborhood contextual characteristics were similar across groups (Table 2). Each selected neighborhood characteristic showed no significant association with a UF diagnosis (Figure 1F). Spearman's correlation of the six neighborhood characteristics showed moderate correlations between several. Spearman's correlation coefficient indicated a value of 0.82 between the hardship index and social vulnerability and 0.63 between the hardship index and neighborhood safety (Figure 2). When stratified by individual-level variables, race, and household income status, the six neighborhood characteristics did not have a statistically significant impact on the odds of a UF diagnosis. When adjusted for age, traffic intensity was slightly protective against a UF diagnosis.

Table 2. Summary of Neighborhood Characteristics.

Neighborhood Characteristic, Median (Interquartile Range)				
	Entire Sample (n = 602)	Fibroid Diagnosis (n = 127)	No Fibroid Diagnosis (n = 475)	*p*-Value
Hardship Index	83.1 (75.3–89.3)	83.1 (57.3–86.9)	83.1 (75.3–89.8)	0.338
Neighborhood safety	47.1 (33.6–58.2)	47.5 (36.5–59.2)	46.3 (33.6–58.2)	0.130
Low food access	36.9 (22.3–63.5)	36.9 (22.3–63.5)	36.9 (22.3–63.5)	0.768
Traffic Intensity	615.3 (411.5–1630.2)	563.1 (411.5–1013.0)	619.2 (411.5–1630.2)	0.031
Social vulnerability	81.5 (72.7–83.5)	81.5 (69.4–82.6)	81.5 (74.0–83.5)	0.284
Received needed care	77.2 (72.7–86.5)	79.3 (74.6–87.6)	77.2 (72.7–86.2)	0.143

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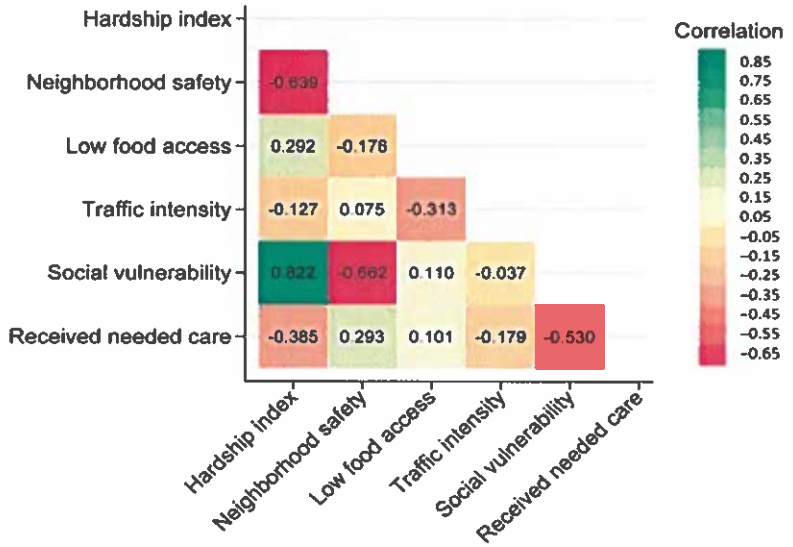

Figure 2. Spearman correlation of Neighborhood contextual variables. Neighborhood contextual factors are categorized into interquartile ranges. Median hardship index (score), neighborhood safety rate (% of adults), low food access (% of residents), traffic intensity (distance-weighted vehicles), social vulnerability index, and received needed care rate (% of adults).

3.3. Environmental Variables

PM2.5 was associated with decreased odds of a UF diagnosis (OR, 0.20; 95% CI, 0.04 to 0.97). DSLPM exposure decreased the odds of UF diagnosis (OR, 0.33; 95% CI, 0.13 to 0.87). Ozone levels did not follow a normal distribution, and median concentration exposures were similar in both groups at 45.409 $\mu g/m^3$. Additionally, ozone exposure decreased the odds of a UF diagnosis, although the effect was not statistically significant (OR, 0.69; 95% CI, 0.33 to 1.41). Average PTRAP exposure was 9.825 $\mu g/m^3$, and it did not significantly impact the odds of a UF diagnosis in our sample (Figure 1E). Of note, other multivariable analyses performed did not meet the Hosmer–Lemeshow goodness of fit test.

4. Discussion

In recent years, considerable attention has been given to understanding the role of social, economic, and environmental factors on health inequity [20]. This study explores UF prevalence among predominantly Black urban residents in Chicago, considering individual, neighborhood, and environmental factors. Chicago's unique features—socioeconomic profile, demographic composition, high traffic, and industrial presence, leading to poor air quality—make it an ideal location for assessing UF prevalence [15]. However, these features affect the generalizability of our findings. Furthermore, the small sample size, relatively narrow exposure distribution, and oversampling of non-Hispanic Blacks, who are disproportionately impacted by UFs, may explain the lack of statistically significant findings.

In this study, 85% of participants were non-Hispanic Blacks. Black participants had a higher likelihood of a UF diagnosis, and we observed a positive correlation between a UF diagnosis and lifestyle and demographic factors such as regular alcohol use, secondhand smoke exposure, elevated BMI, and infrequent exercise. These findings are consistent with well-established data [1,3,5,9]. The association we found between an active lifestyle and higher odds of a UF diagnosis was unexpected and may be attributable to physical activity

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overestimation bias since our classification process was based on participants' self-report of engagement in activities [21]. Forty-two percent of participants reported concerns about crime and violence, which impacted their ability to engage in outdoor physical activity and affected their daily lives. Participants with these concerns had higher odds of a UF diagnosis. Despite the lack of statistical significance, which could be attributed to an overall small sample size, this correlation is expected because crime and violence are a significant source of chronic stress, which can lead to allostatic load and a subsequent pro-inflammatory state [22]. Chronic inflammation has been implicated in the development of UFs and may be a critical contributing factor to the racial disparity observed in UF diagnoses. The increased odds of a UF diagnosis in participants reporting a history of pregnancy loss and hysterectomy are consistent with published data and underscore the substantial morbidity associated with UFs, as well as their negative impact on quality of life [1,23]. Although research has suggested that pregnancy protects against UF occurrence [24], our study found that participants who had been pregnant before had higher odds of a UF diagnosis. This finding could be due to the common occurrence of UF diagnoses during pregnancy.

Neighborhood characteristics, independently and stratified by individual-level variables (race and household income), did not significantly influence UF diagnoses. This was an unexpected finding, and we suspect it is due to an overall low sample size, i.e., Type II error [25]. Furthermore, no statistically significant correlation was found between ozone or PTRAF exposure and UF diagnoses, whereas DSLPM and PM2.5 showed statistically significant negative correlations with UF diagnosis. These findings were not as expected because previous studies have explored the association between air pollutants and UFs, with some reporting a modest increased risk of UF with ozone and PM2.5 exposure [12–14]. Our findings may differ from prior studies due to overall lower levels and narrower ranges of ozone (44–46 $\mu g/m^3$ vs. 50.74–71.04 $\mu g/m^3$ in Black Woman's Health Study) and average PM2.5 (9.82 $\mu g/m^3$ vs. 13.6 $\mu g/m^3$ in Black Woman's Health Study and 15.3 $\mu g/m^3$ in The Nurses' Health Study II). Although our findings do not invalidate previous data, they suggest a possible threshold exposure level where UF risk increases, and larger variations in exposure levels may allow differences to be observed, while smaller variations reduce the ability to detect such differences.

4.1. Strengths and Limitations

This study has several strengths. First, the disadvantaged group most impacted by UF is adequately represented in our study sample. Second, our data source, COMPASS, provides access to specific neighborhood characteristics using participant-supplied addresses instead of proxy variables. Third, this paper investigates an important and understudied issue of the social and environmental causes of health inequity in UF prevalence. There are several limitations of this study. First, despite access to a large cohort, we performed a cross-sectional analysis of a relatively small sample of 602 participants who completed the survey module assessing UF diagnosis. The analyzed sample was not nationally or geographically representative, and although the over-representation of disadvantaged groups is a strength, it limits the generalizability of our study findings. Second, the age and report of UF diagnosis are not validated by medical data. This, along with other findings, may be influenced by questionnaire and recall bias [26]. Although validation of fibroid diagnosis is preferred, previous data suggests that patient-report is accurate for over 90% of patients with UF [27,28]. To mitigate these limitations for future studies using COMPASS, we will request that a UF diagnosis be included in all surveys, as well as questions addressing age at diagnosis and verification of an image-confirmed diagnosis. Lastly, the lack of a temporal association between air pollutant data collection and the date of UF diagnosis, due to the nature of survey response collection, limits the interpretation of our findings on the impact of air pollution exposure on a UF diagnosis. Future studies with larger sample sizes, wider exposure distributions, inclusion of medical record data, and more comprehensive data collection methods will contribute to a deeper understanding of the factors influencing UF diagnoses.

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4.2. Further Research

To reflect the association more accurately between exposures and disease diagnosis, studies evaluating the impact of socioeconomic, lifestyle, and environmental factors on UFs should capture both the age at diagnosis and the duration of environmental exposures leading to or at the time of diagnosis. Additionally, participants from cohorts specifically designed to investigate health conditions, such as UFs, should be sampled for analysis. Alternatively, existing cohorts, such as COMPASS, could be modified accordingly to avoid limited and inaccurate information about the condition in question. Lastly, similar studies using population-based cohorts could enhance heterogeneity and variability within the cohort, therefore improving the generalizability of the study results.

5. Conclusions

The impact of structural and environmental factors on UF development is a growing area of research interest. Our investigation of this relationship in a predominantly Black Chicago-based cohort, which includes individuals residing in historically disenfranchised communities of South Chicago, did not reveal significant associations between these structural drivers and UF prevalence. However, our study provides foundational insights into the cohort that we queried and identifies an opportunity to leverage an existing longitudinal cohort study by expanding its variables to include gynecologic-specific data that would improve the robustness of future analysis. Future analysis with more robust data may allow us to determine if there is a significant association between structural and environmental variables and UF prevalence. Identifying this relationship, if it exists, would provide a justifiable platform to pursue policy changes.

Author Contributions: O.S.M.-L. recognized the educational value of this study, assembled the research team, and coordinated the execution of the study. The COMPASS study protocol was designed by H.A. K.O. directs the University of Chicago Comprehensive Cancer Center (UCCC), which provides funding support for COMPASS. B.A.-K. oversaw field operations, and N.R. oversaw the biosample processing and biobanking. H.A. and B.A.-K. oversaw engagement. N.R. performed the data quality control and the statistical analysis for the COMPASS study and abstracted the relevant data for the fibroid prevalence study. Data cleaning of the abstracted COMPASS study data was performed by S.N. and T.T. The fibroid prevalence study protocol was designed by O.S.M.-L., S.N. and T.T. Data analysis for the fibroid prevalence study was performed by C.L. The first draft of the manuscript was written by S.N., T.T., C.L. and O.S.M.-L. All authors have read and agreed to the published version of the manuscript.

Funding: This research was supported by funding from NIH grants P30ES027792 and U2RTW010122, and the University of Chicago Medicine Comprehensive Cancer Center. Additionally, the environmental linkage was funded by NIEHS Grant #P30 ES027792.

Institutional Review Board Statement: All study procedures and materials were reviewed and approved by the University of Chicago Biological Sciences Division Institutional Review Board Committee A (approval IRB12-1660).

Informed Consent Statement: Informed consent was not required for this study.

Data Availability Statement: Data are available upon reasonable request. COMPASS will continue to collect a rich set of data on multiple exposure domains and health outcomes. For more information, refer to the website compass.uchicago.edu (accessed on 2 December 2023). Researchers interested in collaboration are invited to propose research questions based on the data available within COMPASS or to submit a request for additional data collection. Requests can be submitted electronically on the COMPASS website and will be reviewed by the COMPASS scientific board. The COMPASS study team is particularly interested in collaborations that will enhance research methods for this type of work, assess the impact of environmental exposure, highlight exposures of key significance in urban communities, and address health issues of concern in Chicago and other urban centers.

Acknowledgments: We thank the dedicated COMPASS field staff and community partners for their support of this work.

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Conflicts of Interest: The authors declare no conflict of interest.

Abbreviations

UF	Uterine Fibroid
COMPASS	Chicago Multiethnic Prevention and Surveillance Study
OR	Odds Ratio
CI	Confidence Interval
BMI	Body Mass Index
PM	2.5 Particulate Matter 2.5
NIH	National Institute of Health
NCI	National Cancer Institute
CHA	Chicago Health Atlas
EJSCREEN	Environmental Justice Screening
FIPS	Federal Information Processing Standards
SD	Standard Deviation
IQR	Interquartile Range
WQS	Weighted Quantile Sum
DSLPM	Diesel Particulate Matter
PTRAF	Proximity to Traffic

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ORIGINAL ARTICLE

Uterine-Artery Embolization versus Surgery for Symptomatic Uterine Fibroids

The REST Investigators*

ABSTRACT

BACKGROUND

The efficacy and safety of uterine-artery embolization, as compared with standard surgical methods, for the treatment of symptomatic uterine fibroids remain uncertain.

METHODS

We conducted a randomized trial comparing uterine-artery embolization and surgery in women with symptomatic uterine fibroids. The primary outcome was quality of life at 1 year of follow-up, as measured by the Medical Outcomes Study 36-Item Short-Form General Health Survey (SF-36).

RESULTS

Patients were randomly assigned in a 2:1 ratio to undergo either uterine-artery embolization or surgery, with 106 patients undergoing embolization and 51 undergoing surgery (43 hysterectomies and 8 myomectomies). There were no significant differences between groups in any of the eight components of the SF-36 scores at 1 year. The embolization group had a shorter median duration of hospitalization than the surgical group (1 day vs. 5 days, $P<0.001$) and a shorter time before returning to work ($P<0.001$). At 1 year, symptom scores were better in the surgical group ($P=0.03$). During the first year of follow-up, there were 13 major adverse events in the embolization group (12%) and 10 in the surgical group (20%) ($P=0.22$), mostly related to the intervention. Ten patients in the embolization group (9%) required repeated embolization or hysterectomy for inadequate symptom control. After the first year of follow-up, 14 women in the embolization group (13%) required hospitalization, 3 of them for major adverse events and 11 for reintervention for treatment failure.

CONCLUSIONS

In women with symptomatic fibroids, the faster recovery after embolization must be weighed against the need for further treatment in a minority of patients. (ISRCTN.org number, ISRCTN23023665.)

The Writing Committee of the Randomized Trial of Embolization versus Surgical Treatment for Fibroids consisted of Richard D. Edwards, M.B., Ch.B., and Jonathan G. Moss, M.B., Ch.B., Gartnavel Hospital; Mary Ann Lumsden, M.D., Olivia Wu, Ph.D., and Lilian S. Murray, Ph.D., University of Glasgow — all in Glasgow, Scotland; and Sara Twaddle, Ph.D., Scottish Intercollegiate Guidelines Network, and Gordon D. Murray, Ph.D., University of Edinburgh Medical School — both in Edinburgh. Address reprint requests to Dr. Moss at the Department of Radiology, North Glasgow Hospitals, Gartnavel Hospital, 1053 Great Western Rd., Glasgow G12 OYN, United Kingdom, or at jon.moss@northglasgow.scot.nhs.uk.

*Investigators in the REST trial are listed in the Appendix.

N Engl J Med 2007;356:360-70.

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UTERINE-ARTERY EMBOLIZATION VERSUS SURGERY FOR SYMPTOMATIC UTERINE FIBROIDS

UTERINE FIBROIDS ARE THE MOST COMMON type of tumor in the female reproductive system. The presence of these tumors may cause menstrual disorder and can be associated with subfertility, miscarriage, and pressure effects.[1] For women who no longer plan to give birth, the established treatment is hysterectomy. In the United Kingdom, approximately 42,500 hysterectomies are performed annually, with approximately 30% indicated for fibroids (the second-most-frequent indication).[2] For women wishing to maintain their fertility, myomectomy is the principal option.

Uterine-artery embolization was introduced in 1995 as an alternative technique for treating fibroids.[3] Since then it has become increasingly accepted as a minimally invasive, uterine-sparing procedure, and more than 100,000 procedures have been performed during the past decade, mainly in the United States and Western Europe.[4] Early analysis of an open, prospective, voluntary U.S. registry including 3160 patients revealed major complications in 5.5% of patients at 30 days, with 0.1% requiring a hysterectomy.[5] In the United Kingdom, the National Institute for Health and Clinical Excellence issued guidelines in October 2004, stating that the procedure appeared to be safe for routine use and that the majority of patients have short-term symptomatic relief.[6] However, there has been a need for a careful assessment of the effects of the procedure on quality of life, particularly in comparison with standard surgical approaches.[7] We designed a randomized trial comparing uterine-artery embolization and surgery to assess quality of life and other outcomes at 1 year of follow-up.

METHODS

We conducted the trial in 27 hospitals in the United Kingdom. Each hospital was associated with one of four regional centers. Patients were randomly assigned to study groups from November 2000 through May 2004. The 12-month follow-up was completed in September 2005.

The study was approved by the Multicenter Research Ethics Committee and local ethics committees at each center. All patients provided written informed consent. Potential patients were provided with written information describing the study and possible risks, including the unknown effect of embolization on subsequent pregnancy.

Experienced interventional radiologists performed the embolizations; patients were referred to specialist centers from district units in which embolization was not available. Hysterectomy and myomectomy were performed at each local center.

PATIENTS

Women at least 18 years old were eligible if they had one or more fibroids of more than 2 cm in diameter that could be adequately visualized with the use of magnetic resonance imaging (MRI), caused symptoms (such as menorrhagia or pelvic pain and pressure), and were considered by the patient's physician to justify surgical treatment. Exclusion criteria included a contraindication to MRI, severe allergy to iodinated contrast media, subserosal pedunculated fibroids, recent or ongoing pelvic inflammatory disease, pregnancy, and any contraindication to surgery. There was no upper limit on the size or number of fibroids.

PROCEDURES

Patients were randomly assigned to study groups according to a computer-generated schedule (permuted blocks) held by the trial coordinator. Randomization was stratified by center and was performed in a 2:1 ratio, with twice as many patients allocated to the embolization group as to the surgical group. This design allowed better characterization of the outcomes of the embolization procedure with minimal reduction in statistical power. The method of hysterectomy or myomectomy was not specified; the choice between these options depended on whether the patient wished to retain her uterus for fertility or other reasons. Both operations were included, since virtually all operations for fibroids are performed by the open route, allowing appropriate comparison of outcomes. The technique for embolization was also not specified, but both uterine arteries had to be embolized and the particle size of the embolic agent was standardized (500 to 710 μm).

OUTCOME MEASURES

The primary outcome measure was quality of life, as assessed at 12 months on the Medical Outcomes Study 36-Item Short-Form General Health Survey (SF-36), with scores ranging from 0 to 100, with higher scores indicating better function. This assessment has been validated in women with menorrhagia.[8] Secondary outcomes included an assessment of findings on the EuroQol-5D ques-

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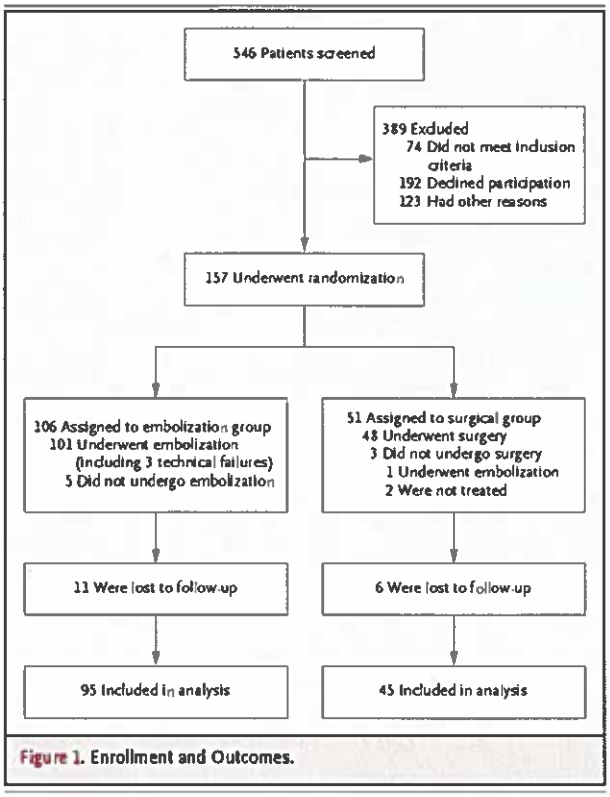

Figure 1. Enrollment and Outcomes.

tionnaire, an instrument used to measure preferences for certain health outcomes, including hysterectomy,[9,10] with a range of scores paralleling that of the SF-36; an 11-point symptom score, ranging from −5 (markedly worse) to +5 (markedly better); the time until the resumption of usual activities; a satisfaction score measuring whether patients would recommend the procedure to a friend; a linear-analogue pain score at 24 hours; the presence or absence of complications; and treatment failure, defined as the need for subsequent intervention for symptom control, including hysterectomy or repeated embolization.

Complications were graded with the use of the classification system of the Society of Interventional Radiology, as recommended in the Standards of Practice[11] as follows: no therapy required or no consequence (grade 1); nominal therapy required or no consequence, including overnight admission for observation only (grade 2); therapy required, including minor hospitalization of less than 48 hours (grade 3); major therapy required, including an unplanned increase in the level of care or hospitalization for at least 48 hours (grade 4); and permanent adverse sequelae (grade 5). Grades 1 and 2 were considered to be minor; grades 3 through 5 were considered to be major. Two of the investigators (a gynecologist and a radiologist) independently categorized the grades of complications. In 56% of cases, the investigators were in complete agreement; in 91% of cases, they were in agreement to within one grade of complication. In discordant cases, the worse grade was used. Major adverse events included any major complication, a life-threatening event, initial or prolonged hospitalization, an intervention required to prevent permanent impairment or damage, and death. Treatment failures requiring subsequent intervention were considered separately.

We assessed outcome measures (with the exception of the 24-hour pain score) at 1, 6, 12, and 21 months and annually thereafter. In this study, we present the 12-month results, with two exceptions: major adverse events requiring hospitalization and subsequent intervention for treatment failure, which are reported through September 2005 (maximum follow-up, 58 months).

ECONOMIC ANALYSIS

We prospectively collected data on the total use of financial resources up to 12 months after treatment. These data included the time in the operating room and recovery room, the total length of stay in the hospital, outpatient visits associated with the procedure, treatment failure, and any associated complications. We obtained unit costs for all resources used from routinely collected data and published literature; we used such data to determine the direct health care costs associated with each patient from the perspective of the National Health Service. Since the trial showed no significant differences between groups in the primary outcome, we considered the appropriate form of economic evaluation to be a cost-minimization analysis.[12] We calculated the 95% confidence intervals (CIs) for the differences in costs between groups with the use of the bias-corrected and accelerated bootstrap method.[13] We performed one-way sensitivity analysis on key unit cost components by varying one measure at a time.

STATISTICAL ANALYSIS

We analyzed all patients in the group to which they were randomly assigned, regardless of the treatment actually received. Analysis of covariance was used to compare quality-of-life scores (on the

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basis of results on the SF-36 and EuroQol questionnaires) between groups, adjusting for baseline values. Other comparisons between groups were made with the use of a two-sided Student's t-test and the Mann–Whitney test for continuous data and the chi-square test for categorical data. The original power calculation required the enrollment of 200 patients to give a power of 90% to detect a difference of 10 points in the SF-36 score at 12 months (the primary end point) at the 0.05 significance level. Because of slower-than-expected recruitment, the decision was subsequently made to reduce the power to 80%, which required the enrollment of 150 patients.

An independent data and safety monitoring committee reviewed the results and serious adverse events every 12 months. The panel followed the highly conservative Haybittle–Peto approach of requiring a significance level of less than 0.001 in the comparison between groups before making any recommendation to terminate the trial prematurely.[14]

The manufacturers of the embolic agents used in the study (William Cook Europe, Cordis, and Biocompatibles) had no role in the design of the study; data collection, analysis, and interpretation; or the writing of the final report. The Writing Committee members assume responsibility for the accuracy and completeness of the data and for the overall content and integrity of the article.

RESULTS

A total of 157 women were randomly assigned to study groups: 106 to undergo uterine-artery embolization and 51 to undergo surgery, including 43 hysterectomies and 8 myomectomies (Fig. 1). Eight patients (5%) did not receive their allocated treatments (five in the embolization group and three in the surgery group). In addition, there was one technical failure in the surgical group (a myomectomy converted to hysterectomy owing to technical difficulties) and there were three technical failures in the embolization group (owing to difficulty in the identification or catheterization of one or both uterine arteries). All the hysterectomies and myomectomies were performed through an abdominal incision. The groups were well matched at baseline (Table 1).

Table 1. Baseline Characteristics of the Patients.*

Characteristic	Embolization Group (N = 106)	Surgical Group (N = 51)	P Value
Age — yr	43.6±5.5	43.3±7.1	0.77
Largest fibroid diameter — cm	7.5±3.0	8.5±3.9	0.12
Uterine volume — ml	579±447	701±627	0.23
SF-36 score†			
Physical function	82±19	77±20	0.16
Physical role	51±41	45±42	0.35
Bodily pain	52±22	50±22	0.60
General health	61±19	60±23	0.92
Vitality	41±22	42±23	0.93
Social function	63±27	58±30	0.34
Emotional role	60±43	57±43	0.76
Mental health	63±18	63±22	0.91
EuroQol score†	70±16	63±20	0.04
Main presenting symptom — no. (%)			0.92
No. of patients	102	50	
Bleeding	56 (55)	29 (58)	
Pain	19 (19)	7 (14)	
Pressure	23 (23)	12 (24)	
Other	4 (4)	2 (4)	

* All study participants were premenopausal. Plus–minus values are means ±SD. SF-36 denotes Medical Outcomes Study 36-Item Short-Form General Health Survey.
† Scores on the SF-36 and EuroQol range from 0 (worst possible) to 100 (best possible).

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Table 2. Effects of Uterine-Artery Embolization and Surgery on Measures of Quality of Life, Symptoms, and Resumption of Usual Activities.*

Effect	Embolization Group (N=106)	Surgical Group (N=51)	Absolute Difference (95% CI)†	P Value
SF-36‡				
At 1 mo				
No. of patients	95	47		
Score				
Physical function	85±16	57±25	−26 (−32 to −20)	<0.001
Physical role	37±44	11±24	−25 (−38 to −12)	<0.001
Bodily pain	50±22	44±24	−6 (−14 to 2)	0.16
General health	70±19	74±17	4 (−1 to 10)	0.13
Vitality	47±22	42±24	−6 (−13 to 1)	0.11
Social function	64±27	44±29	−19 (−28 to −9)	<0.001
Emotional role	72±41	64±44	−7 (−22 to 7)	0.32
Mental health	72±17	74±18	2 (−3 to 8)	0.39
At 12 mo				
No. of patients	95	47		
Score				
Physical function	92±14	89±20	0 (−6 to 5)	0.85
Physical role	76±40	81±34	7 (−7 to 20)	0.33
Bodily pain	76±23	80±26	4 (−4 to 13)	0.28
General health	74±20	79±17	6 (0 to 12)	0.07
Vitality	62±21	67±22	4 (−3 to 11)	0.26
Social function	84±23	87±26	4 (−4 to 12)	0.35
Emotional role	81±35	87±30	7 (−4 to 18)	0.22
Mental health	76±17	76±21	−1 (−7 to 5)	0.80
EuroQol‡				
At 1 mo				
No. of patients	92	47		
Score	74±17	67±19	−4 (−9 to 2)	0.24
At 12 mo				
No. of patients	93	45		
Score	82±16	83±14	4 (−2 to 9)	0.18
24-hour pain score§				
No. of patients	99	49		
Score	3.0±2.1	4.6±2.3	1.6 (0.8 to 2.3)	<0.001
Symptom score¶				
At 1 mo				
No. of patients	98	48		
Score	1.5±2.4	2.8±2.6	1.3 (0.4 to 2.2)	0.004
At 12 mo				
No. of patients	95	45		
Score	3.6±2.0	4.3±1.7	0.7 (0.1 to 1.4)	0.03

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Table 2. (Continued.)

Effect	Embolization Group (N=106)	Surgical Group (N=51)	Percent Difference (95% CI)†	P Value
Patients who would recommend treatment to a friend				
At 1 mo — no./total no. (%)	74/97 (76)	37/48 (77)	1 (−14 to 15)	0.92
At 12 mo — no./total no. (%)	84/95 (88)	42/45 (93)	5 (5 to 15)	0.32
Hospital stay and time until resumption of usual activities			95% CI‖	
Hospital stay — day				
Median	1	5	3 to 4	<0.001
Interquartile range	1–2	3–6		
Made cup of tea — day				
Median	2	6	3 to 5	<0.001
Interquartile range	1–3	4–11		
Made meal — day				
Median	6	17	6 to 14	<0.001
Interquartile range	3–9	10–23		
Drove car — day				
Median	8	34	22 to 30	<0.001
Interquartile range	5–10	27–43		
Returned to work — day				
Median	20	62	28 to 53	<0.001
Interquartile range	14–30	39–90		
Had sexual intercourse — day				
Median	21	53	18 to 45	<0.001
Interquartile range	13–31	29–91		

* Plus–minus values are means ±SD. CI denotes confidence interval, and SF-36 Medical Outcomes Study 36-Item Short-Form General Health Survey.
† For the differences in quality-of-life scores (on the SF-36 and EuroQol) between the surgical group and the embolization group, the analysis of covariance adjusted for baseline values, so the differences between the groups are not the simple numerical differences. Negative values indicate higher scores in the embolization group, and positive numbers indicate higher scores in the surgical group.
‡ Scores on the SF-36 and EuroQol range from 0 (worst possible) to 100 (best possible).
§ Scores on the 24-hour pain scale range from 0 (no pain) to 10 (continuous, severe pain) on a continuous scale.
¶ Symptom scores range from −5 (markedly worse) to +5 (markedly better) on an integer scale.
‖ The 95% CIs are for the difference in medians. Data are excluded for patients who did not have a response to a category (e.g., nondrivers).

PRIMARY OUTCOME

The primary outcome measure (the SF-36 quality-of-life score at 12 months) was available for 140 of the 157 women (89%). The results on the SF-36 and EuroQol at 1 and 12 months are shown in Table 2. There were no significant differences between groups in any of the eight components of the SF-36 at 12 months, although at 1 month, the embolization group had significantly greater improvement in scores than the surgery group for the physical function, social function, and physical-role components.

SECONDARY OUTCOMES

Women in the surgical group had a significantly higher pain score at 24 hours (Table 2). Symptom scores at 1 and 12 months after the procedure were significantly better in the surgical group. At 12 months, the percentage of women who reported that they would recommend their treatment to a friend was high in both treatment groups (93% in the surgical group and 88% in the embolization group) (P=0.32).

The median hospital stay after uterine-artery embolization was significantly shorter than that

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after surgery (1 day vs. 5 days, P<0.001). The median time until patients could resume all recorded usual activities was significantly lower in the embolization group (Table 2).

MINOR COMPLICATIONS

Minor complications were reported by 36 women (34%) in the embolization group and 10 (20%) in the surgical group (P=0.06) (Table 3). Minor complications were usually related to the postembolization syndrome (52%), which includes pyrexia, pain, and elevated inflammatory markers, in the embolization group and to minor infections (25%) in the surgical group.

MAJOR ADVERSE EVENTS

There were 16 major adverse events (15%) in the embolization group, as compared with 10 (20%) in the surgical group during a median follow-up of 32 months (interquartile range, 23 to 41) (Table 3). When we categorized these events with respect to the timing of their occurrence (i.e., during the hospital stay, during the first year of follow-up, or after the first year), 8 of the 10 major adverse events in the surgical group occurred during the hospital stay, whereas 15 of the 16 events in the embolization group occurred after discharge from the hospital.

TREATMENT FAILURES

Twenty-one patients (20%) in the embolization group required an additional invasive procedure (hysterectomy or repeated uterine-artery embolization) for continued or recurrent symptoms, 10 during the first 12 months of follow-up (2 of which were due to technical failures) and 11 subsequently. In the surgical group, there was one conversion of myomectomy to hysterectomy at the time of the primary procedure.

ECONOMIC ANALYSIS

Uterine-artery embolization was associated with a lower use of resources than was surgery at the initial hospitalization. However, during the 1-year follow-up period, when compared with surgery, embolization was associated with more imaging studies and a longer mean hospital stay.

Table 4 shows the results of the cost-minimization analysis and one-way sensitivity analysis.[15-18] Uterine-artery embolization was associated with total costs significantly lower than those for surgery (mean difference, £951 [$1,712 at an exchange rate of £1=$1.80]; 95% CI, £329 to £1480 [$592 to $2,664], suggesting that at 1 year, embolization was more cost-effective than surgery for patients with symptomatic uterine fibroids, from the perspective of the National Health Service. Sensitivity analyses showed the result was robust when assumptions were varied around the cost of MRI and the embolization agent. The results were sensitive to the cost per inpatient-day, with no significant difference in costs between the two procedures when the cost per inpatient-day was halved. Threshold analysis indicated that uterine-artery embolization was more cost-effective over a 12-month period only if the cost per inpatient-day exceeded £291 ($524).

OTHER OUTCOMES

Through September 2005, eight pregnancies had occurred in five women (seven in the embolization group and one in the myomectomy group). Four of the pregnancies resulted in miscarriage, three in successful live births (two by cesarean section, including one patient from each group, and one spontaneous vertex delivery), and one intrauterine death of the fetus at 33 weeks (with no abnormalities found on postmortem examination).

DISCUSSION

In this randomized trial comparing uterine-artery embolization with standard surgical treatment for women with symptomatic fibroids, we found no significant differences between the groups in measures of quality of life at 12 months, although women in both groups had substantial improvements in each component of the SF-36 score relative to baseline. In contrast, the adverse-event profiles were very different. Surgery was associated with the expected acute morbidity, but only one major adverse event was recorded after the initial hospital stay. Uterine-artery embolization was associated with a significantly faster recovery, including the resumption of usual activities.

Rates of minor complications or major adverse events did not differ significantly between the study groups, although the nature and timing of these events varied between groups; major adverse events in the surgical group typically occurred during the hospital stay, whereas in the embolization group, such events more commonly occurred after hospital discharge. Of note, three of the major adverse events in the embolization group

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Table 3. Minor Complications within First Year and Major Adverse Events and Interventions for Treatment Failure Occurring during Median Follow-up of 32 Months.*

Variable	Embolization Group (N = 106)	Surgical Group (N = 51)
Minor complications at 1 yr		
Patients reporting any minor complication — no. (%)	36 (34)	10 (20)
Complications reported		
Total number	50	16
Type of complication	Postembolization syndrome (26 patients), vaginal discharge (9), sepsis (6), other (9)	Infection (4 patients), hemorrhage (3), other (9)
Major adverse events		
Patients reporting any adverse event — no. (%)	16 (15)	10 (20)
During hospital stay		
Total number	1	8
Type of event	Severe vasovagal event requiring atropine (1 patient)	Operative hemorrhage, with 1 requiring left oophorectomy (2 patients); anesthetic complication (2); wound infection (2); wound hematoma (1); urinary retention (1)
During first year of follow-up		
Total number	12	2
Type of event	Breast cancer — both cases diagnosed 2 mo after treatment (2 patients); pain and pelvic infection requiring readmission at 1 and 4 wk (2); severe pain and fibroid expulsion at 3, 4, and 6 wk (3); hematometria at 6 mo — not treated (1); persistent severe pain requiring hysterectomy at 8 mo — necrotic fibroid tissue seen on pathological analysis (1); pelvic abscess requiring hysterectomy at 10 mo (1); temporary amenorrhea for 5 and 9 mo (2)	Wound exploration under general anesthetic (1 patient), wound infection at 3 wk (1)
After first year of follow-up		
Total number	3	0
Type of event	Death from adrenal cancer — diagnosis at 12 mo and death at 13 mo (1 patient); severe pain and fibroid expulsion at 13 mo (1); severe, persistent pain requiring hysterectomy at 15 mo — necrotic fibroid tissue seen on pathological analysis (1)	
Interventions for treatment failure		
Patients reporting any intervention — no. (%)	21 (20)	1 (2)
During hospital stay		
Total number	2	1
Type of event	Technical failure of procedure requiring hysterectomy (2 patients)	Operative complication requiring conversion of myomectomy to hysterectomy (1 patient)
During first year of follow-up		
Total number	8	0
Type of event	Hysterectomy (4 patients), repeated embolization (4)	
After first year of follow-up		
Total number	11	0
Type of event	Hysterectomy (8 patients), repeated embolization (3)	

* For major adverse events after 1 year, only those requiring hospitalization are reported. P = 0.047 for the comparison between the embolization group and the surgical group for minor complications. P = 0.22 for the comparison between the two study groups for major adverse events during the first year. The interquartile range for major adverse events and reinterventions for treatment failure was 23 to 41 months.

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Table 4. Results of Cost-Minimization Analysis and Sensitivity Analysis.*

Variable	Embolization Group (N=106)	Surgical Group (N=51)	Difference†
		mean (95% CI)	
Cost-minimization analysis			
Mean cost per patient per year — £	1727 (1511 to 1943)	2673 (2402 to 2944)	951 (329 to 1480)
Mean cost excluding patients with missing data			
Number of patients	93	44	
Cost per patient — £	1751 (1522 to 1980)	2702 (2414 to 2989)	948 (398 to 1432)
Sensitivity analysis‡			
Cost of MRI and ultrasonography doubled — £	2027 (1811 to 2242)	2683 (2414 to 2952)	658 (131 to 1137)
Cost of MRI and ultrasonography doubled, plus cost of embolization agent (£95) — £	2098 (1880 to 2316)	2684 (2415 to 2952)	599 (41 to 1186)
Cost of hospital stay reduced to 65% (£316) — £	1379 (1233 to 1525)	1844 (1700 to 2018)	468 (113 to 828)
Cost per inpatient day reduced to 50% (£243) — £	1229 (1110 to 1348)	1489 (1349 to 1628)	257 (−89 to 571)

* £1.00 equals $1.80. Calculations were based on the following unit-cost estimates updated to 2004 prices: uterine-artery embolization, £1.53 per minute; surgery, £3.08 per minute; embolic agent, £75 per bottle (times four bottles); hospital stay, £485.55 per day; magnetic resonance imaging (MRI), £152.53 per scan; ultrasonography, £17.50 per scan; and outpatient consultation, £77 per visit.

† The differences in costs between the surgical group and the embolization group were calculated with the use of a bootstrap method, so the differences between the groups are not simple numerical ones.

‡ One-way sensitivity analyses were performed on key unit-cost components by varying one measure at a time.

were cancers (two breast cancers, both detected within 2 months after the intervention, and one adrenal cancer), which were highly unlikely to be related to treatment.

At 1 year, however, 10 of the 106 women in the embolization group had required a secondary intervention to treat persistent or recurrent symptoms. After the first year of follow-up, 11 additional women were readmitted for the same indication. These findings are consistent with data from uncontrolled case series indicating complications and treatment failures up to 48 months after embolization.[19,20]

The cost-minimization analysis showed that at 1 year, embolization was more cost-effective than surgery. This finding supports that of one other study addressing the cost-effectiveness of uterine-artery embolization versus surgery.[21] Ongoing follow-up will further assess the efficacy and cost-effectiveness of embolization.

We used a "pragmatic trial" design, in that the particular surgical interventions and technical aspects of the procedures were not dictated by protocol. We included women undergoing either hysterectomy or myomectomy in the surgical group, although in fact only eight women underwent myomectomy. Our primary outcome measure, the SF-36 score, did not take specific fibroid-related symptoms into account, although it was sensitive to changes in quality of life that resulted from successful treatment of menstrual symptoms.[8] This fact is important, given the cyclical nature of the patients' menstrual problems. We did not collect data on loss of menstrual blood; comparisons of this measure between groups would not be meaningful, given that only eight women in the surgical group underwent myomectomy.

Two other randomized, controlled trials compared uterine-artery embolization with hysterectomy.[22,23] The first study used a controversial randomized-consent methodology,[24] in which women who were randomly assigned to the hysterectomy group were not informed about the study or about the possibility of an alternative treatment (i.e., uterine-artery embolization). In addition, this study was small (enrolling only 57 women) and used the length of hospital stay as the primary outcome measure; hospital stays were significantly shorter after uterine-artery embolization, with similar complication rates in both groups.[22] The second trial comparing embolization and hysterectomy enrolled 177 patients; at 6 weeks after treatment, the embolization group

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had a significantly shorter mean hospital stay but a higher rate of minor complications and readmission.[23]

Limitations of our trial must be acknowledged. The original target number of 200 patients was reduced to 150 because of difficulties in recruitment. Thus, the 95% CIs for the differences between groups indicate that plausible results include as much as a 10-point difference between groups in some components of the SF-36. However, there is no suggestion of clinically important differences. The inclusion of only a small number of patients who underwent myomectomy in the surgical group made it difficult to compare such therapy with uterine-artery embolization. It also suggests that a direct comparison of these two treatments would be difficult to perform unless recruitment involved a very large population base. The use of the time until resumption of usual activities as a secondary outcome must be viewed cautiously, since such an interval could be biased by the patient's expectation (or caregivers' guidance) regarding the time to recovery.

The results of our study make clear that the choice between surgery and uterine-artery embolization for symptomatic uterine fibroids involves tradeoffs. The advantages of embolization — including a significant reduction in the length of the hospital stay and 24-hour pain level and a more rapid return to usual activities — need to be weighed against the risk of treatment failure requiring a second intervention and the possibility, although infrequent, of major late adverse events. Longer-term follow-up is necessary, with attention to the need for repeated intervention, to inform future decision making.

Supported by the Chief Scientist Office of the Scottish Executive, Edinburgh. In addition, Dr. Moss reports receiving on behalf of the trial-management group grants from three companies — William Cook Europe, Cordis, and Biocompatibles — that manufacture embolic agents used in the trial. IBM provided three laptop computers for data collection. The University of Glasgow partly funded a research fellow in gynecology.

Drs. Edwards and Moss report receiving grants from Cordis and William Cook Europe to fund the United Kingdom Interventional Radiology Course; and Dr. Lumsden, lecture fees from Biocompatibles. No other potential conflict of interest relevant to this article was reported.

APPENDIX

In addition to the Writing Committee, the following investigators participated in the RBST trial: Data and Trial Management: L.S. Murray (trial coordinator), H. Dewart, B. Ferrie, M. Khaund, L. Lawrie, D. Lyons, F. McLean. Data Monitoring Committee: I.T. Cameron (chair), H. Critchley, J. Reidy, P. Warner. Trial Management Committee: J.G. Moss (chair), R.D. Edwards, M.A. Lumsden, L.S. Murray (trial coordinator), G.D. Murray, S. Twaddle. Trial Steering Committee: J.G. Moss (chair), R.D. Edwards, M.A. Lumsden, L.S. Murray, G.D. Murray, S. Twaddle, C. West, I. Gillespie, M. Thomson, G. Houston, K. Cooper, P. Thorpe. The following centers and investigators (all in the United Kingdom) participated in the trial: *Aberdeen Royal Infirmary, Aberdeen* — K. Cooper, P. Thorpe; *Bolton Royal Infirmary, Lancashire* — J. Tuck; *Murrayfield Hospital, Edinburgh* — I. Gillespie; *Crosshouse Hospital, Kilmarnock* — G. Irvine; *Eastern General Hospital, Edinburgh* — C. Tay; *Edinburgh Royal Infirmary* — C. West, I. Gillespie; *Falkirk Royal Infirmary, Falkirk* — O. Prabu; *Forth Park, Kirkcaldy* — S. Pinion; *Glasgow Royal Infirmary, Glasgow* — M. Rodger, A. Reid; *Hairmyres Hospital, Lanarkshire* — K. Spowart; *Hull Royal Infirmary, Hull* — J. Killick, A. Nicholson; *Inverclyde Hospital, Greenock* — L. Cassidy; *Monklands Hospital, Lanarkshire* — V. Harper; *Ninewells Hospital, Dundee* — M. Thomson, G. Houston; *Perth Royal Infirmary, Perth* — D. Phillips; *Queen Margaret's Hospital, Dunfermline* — S. Pinion; *Raigmore Hospital, Inverness* — L. Caird, D. Nicholls; *Ross Hall BMI Hospital, Glasgow* — J. Moss; *St. John's Hospital, Livingstone* — P. Dewart; *Southern General Hospital, Glasgow* — M. Carty, G. Urquhart; *Stirling Royal Infirmary, Stirling* — F. Morrison; *Stobhill Hospital, Glasgow* — M. Deeney; *Vale of Leven Hospital, Alexandria* — M. Haxton; and *Western Infirmary, Glasgow* — M.A. Lumsden, N. McMillan.

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MAJOR ARTICLE

Evaluation of a Ureteral Stent Removal Protocol in Adult Kidney Transplant Recipients

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Existing literature on best practices to reduce the risk of infectious complications associated with ureteral stent removal in kidney transplant recipients is limited. Prior to 2021, a formal process surrounding stent removal was not in place at our institution. In June 2021, a stent removal protocol was established. This protocol included the following: obtaining a preprocedure urine culture, prescribing universal culture-directed antimicrobial prophylaxis, earlier stent removal posttransplant, and patient education. We performed a retrospective quasi-experimental study of kidney transplant recipients who had their stents removed between July 2020 and June 2022. The primary outcome was the incidence of infectious complications within 30 days. Infectious complications were defined as urinary tract infection and bacteremia due to urinary source, as well as hospitalization, emergency department visit, or outpatient encounter for possible urinary tract infection. Secondary objectives included infectious and immunologic complications within 30 days to 1 year from transplant. During this study period, 239 adult kidney transplant recipients were included: 88 in the preprotocol group and 151 in the protocol group. The median time to stent removal was shorter in the protocol group (25 vs 36 days, $P < .001$). More patients in the protocol group received preprocedure antibiotics (99% vs 36%, $P < .001$). Infectious complications were higher in the preprotocol group (9% vs 3%, $P = .035$). Overall, the stent removal protocol was associated with fewer infectious complications (odds ratio, 0.18; 95% CI, 0.05–0.73). Further investigation is necessary to determine which individual interventions, if any, drive this benefit.

Keywords. antibiotic; antimicrobial; kidney; organ transplant; prophylaxis.

Ureteral stent insertion at the time of kidney transplantation decreases the risk of urologic complications such as anastomotic leak, stricture, or obstruction [1]. However, the benefits of minimizing mechanical complications should be weighed against the intrinsic risk of microbial colonization and associated urinary tract infections (UTIs) [1–3]. In a study by Alangaden et al, ureteral stenting was one of the strongest predictors of UTI after kidney transplantation, as 71% of patients with stents developed UTI as opposed to 33% of patients without stents ($P < .001$) [3]. While microbial colonization has not been shown to affect long-term graft function, infectious complications after stent removal can cause significant morbidity or mortality in the patient who is immunocompromised [1].

Several factors may increase the risk of infectious complications after stent removal, such as patient comorbidities, anomalies of the urinary tract, urinary obstruction, incomplete bladder emptying, and duration of stent induration [4]. Optimizing modifiable risk factors can potentially decrease complications posttransplant. Existing literature has found earlier stent removal, particularly within 3 weeks posttransplant, to be associated with a decreased incidence of UTIs, with no significant difference in the incidence of major urologic complications when compared with later removal (>3 weeks) [5, 6].

Additionally, the American Urological Association (AUA) best practice guidelines state that antimicrobial prophylaxis may be considered for clinical procedures, including removal of ureteral stents, especially when patient and procedural risk factors are present [7]. The 2022 European Association of Urology guidelines on urologic infections state that asymptomatic bacteriuria is considered a risk factor for infectious complications during ureteral stent placement or exchange; therefore, screening and treatment prior to the procedure are recommended [8].

Prior to 2021, a formal process surrounding stent removal was not in place at our institution and practices varied. In

Received 26 March 2024; editorial decision 29 August 2024; accepted 03 September 2024; published online 5 September 2024

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https://doi.org/10.1093/ofid/ofae510

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2021, a multidisciplinary group was established to develop a standard process surrounding ureteral stent removal after kidney transplantation. The protocol included: removing the stent at 3 weeks posttransplant, obtaining a urine culture within 1 week prior to stent removal, prescribing universal culture-directed antimicrobial prophylaxis, and providing patient education. This study sought to evaluate the impact of this protocol on infectious and immunologic complications following stent removal.

MATERIALS AND METHODS

Study Center

The University of Chicago Medicine (UCM) is an 811-bed academic medical center located on the South Side of Chicago, Illinois. UCM's kidney transplant program performs living and deceased donor kidney transplants. UCM performs around 150 kidney transplants per year. All kidney transplant recipients have a ureteral stent placed at the time of transplant surgery. These stents are later removed via clinic cystoscopy by the urologic surgical team unless the patient has a concurrent need requiring the operating room.

Intervention

Prior to 1 June 2021, there was no standard process for coordination between the urology and transplant nephrology divisions regarding antimicrobial prophylaxis and timing of ureteral stent removal. Ureteral stents were removed by the urology division approximately 4 to 6 weeks posttransplant. In 2021, a multidisciplinary working group was established to develop and implement a standardized stent removal process. This group consisted of physician, advanced practice nurse, and pharmacist representatives from transplant surgery, transplant nephrology, urology, and infectious diseases. The stent removal protocol implemented on 1 June 2021 included the following: (1) removing the stent at 3 weeks posttransplant, (2) obtaining a urine culture within 1 week prior to stent removal, (3) prescribing universal culture-directed antimicrobial prophylaxis, and (4) patient education (Supplementary Appendix 1). Patients with symptomatic UTIs at the time of stent removal were excluded and followed a separate treatment algorithm.

The patient's nephrologist ordered the preprocedure urine culture and antimicrobial prophylaxis. Antibiotic prophylaxis was guided by the preprocedure urine culture (Supplementary Tables 1 and 2). Patients with a positive preprocedure urine culture received a minimum 3 days of antimicrobial prophylaxis prior to the stent removal procedure. Those with a negative urine culture received 24 hours of cephalexin beginning the morning of stent removal (prior to the procedure). For ease of outpatient dosing, cephalexin was selected as an oral equivalent to the cefazolin recommended by the AUA best practice guidelines for transurethral cases, including stent removal [7]. Microbiologic and susceptibility data were not available for this specific patient population at the time. The Infectious Diseases and Antimicrobial Stewardship Program was available to answer questions for culture-directed therapy if the preprocedure urine culture grew an organism that was not covered by recommended therapies. Continuing antibiotics beyond the date of stent removal was not recommended.

Prior to proceeding with stent removal, urology staff screened to ensure that patients had taken the requisite antibiotics. Patients who were not adherent or were unsure of adherence to antibiotic prophylaxis were given intramuscular gentamicin within 30 to 60 minutes prior to the procedure. Removed ureteral stents were sent for microbial analysis. Patient education regarding when to reach out to the urology division for issues or concerns was also developed and reinforced (Supplementary Appendix 1).

Aside from the protocol interventions described so far, no other procedural or UTI management changes were made during the entire study period. Patients maintained routine posttransplant follow-up appointments, in which urinary symptoms were assessed and urine cultures were sent only when there was suspicion for a UTI.

Study Design

This retrospective, single-center, quasi-experimental study evaluated adult kidney transplant recipients at a large academic medical center between 1 July 2020 and 30 June 2022. Patients aged ≥18 years were included if they received an isolated kidney transplant and underwent ureteral stent removal during the study period. Patients were excluded if they died prior to stent removal. Patients who had the stent removed prior to 1 June 2021 (preprotocol group) were compared with those who had the stent removed on or after 1 June 2021 (protocol group).

Outcomes

The primary outcome was the incidence of infectious complications within 30 days after stent removal. Infectious complications were defined as UTI or bacteremia due to urinary source, as well as hospitalization, emergency department visit, or outpatient encounter (ie, clinic visit or telephone note) for possible UTI. UTIs were classified as cystitis or pyelonephritis. Cystitis was defined as bacteriuria and at least 1 of the following symptoms: dysuria, urinary frequency, urinary urgency, or suprapubic pain. Pyelonephritis was defined as bacteriuria and at least 1 of the following: fever, chills, malaise, hemodynamic instability, leukocytosis, flank/allograft pain, or bacteremia with the same organism as in the urine. Bacteremia due to urinary source was defined as a positive blood culture with UTI symptoms. Possible UTI included patients with bacteriuria who did not meet the definition for cystitis or pyelonephritis (ie, absence of a urine culture) but received antibiotics due to suspected

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UTI after other causes were ruled out. Health care utilization was defined as a hospitalization, emergency department visit, or outpatient encounter due to possible UTI.

Secondary objectives were as follows: the incidence of the individual components of the primary composite outcome, acute kidney injury within 30 days after stent removal, biopsy-proven rejection within 1 year posttransplant, and mortality within 1 year posttransplant. Acute kidney injury was defined as an increase in serum creatinine >2 times the posttransplant baseline or a glomerular filtration rate decrease >50%.

Statistical Analysis

Descriptive statistics were calculated for the variables in the primary analysis and included mean (SD) and median (IQR). A *t* test was used to compare normally distributed variables, a Mann-Whitney test for nonnormally distributed variables, and a Fisher exact test for categorical variables between the groups. $P < .05$ was considered statistically significant. Stata version 16.1 was used for all analyses (StataCorp).

Multivariable logistic analyses were performed to identify variables associated with infectious complications, while adjusting for confounding variables. Variables in the bivariate analyses at $P < .2$ were included in the explanatory multivariable model at model entry (Supplementary Table 3). The protocol intervention was forced into the model, without the separate interventions. To limit collinearity, a sensitivity analysis was performed with the separate protocol interventions (ie, time to stent removal, receiving antibiotics within 1 week prior to and on the day of stent removal, and a positive preprocedure urine culture) but without the bundled protocol intervention (Supplementary Table 4).

Based on previously published literature, if a 9% rate of infectious complications is observed in the preprotocol group as compared with 2% in the protocol group, 330 patients would be needed to achieve a power of 0.8 and an alpha of 0.05.

Data were managed in a REDCap database [9]. This study received a formal Determination of Quality Improvement status according to UCM institutional policy. As such, this initiative was deemed not human subjects research and was therefore not reviewed by the institutional review board.

RESULTS

A total of 239 adult kidney transplant recipients with ureteral stent placement were eligible and included in the analysis during the study period. Eighty-eight patients (37%) were in the preprotocol group and 151 (63%) in the protocol group. Baseline characteristics such as age, gender, race, and comorbidities were similar between the groups (Table 1). More patients in the protocol group received antithymocyte globulin (rabbit) as induction immunosuppression. At the time of stent removal, the majority of patients were prescribed prednisone, tacrolimus, and mycophenolate mofetil as maintenance immunosuppression. Patients in the preprotocol group were on average receiving a lower daily dose of prednisone and tacrolimus but higher daily dose of mycophenolate mofetil. Despite the difference in tacrolimus dosing, there was no difference seen in the median trough levels of tacrolimus between the groups. Additional details regarding patients' immunosuppression regimen are summarized in Table 1.

The median time to stent removal from time of transplant was significantly longer in the preprotocol group vs the protocol group (36 vs 25 days, $P < .001$). Within 30 days prior to stent removal, more patients in the protocol group had posttransplant urine cultures performed as compared with the preprotocol group (94% vs 46%, $P < .001$; Table 2). The incidence of positive urine cultures obtained within 30 days prior to stent removal was similar between the groups (12.5% vs 14.2%, $P = .080$). In both groups, the most common organisms growing in the urine culture prior to stent removal were *Enterococcus* species and *Escherichia coli*.

Within 1 week prior to and on the day of stent removal, more patients received antibiotics in the protocol group vs the preprotocol group (99% vs 36%, $P < .001$). The most frequently given antibiotics in both groups were cephalexin and cefazolin. More patients in the protocol group received cephalexin than the preprotocol group (76% vs 25%, $P < .001$). Eight patients in the protocol group grew *Enterococci* on their preprocedure urine culture: 3 received cephalexin because the urine culture results did not return until after stent removal, and 5 received amoxicillin, ampicillin, or amoxicillin-clavulanic acid. There was no difference in the number of patients receiving trimethoprim-sulfamethoxazole (TMP-SMX) for prophylaxis (92% vs 89%, $P = .651$). Following stent removal, antibiotics were continued in 10 patients (11%) in the preprotocol group and 29 (19%) in the postprotocol arm for a median 4 days in both groups (Table 3). Reasons for continuing antibiotics after stent removal primarily included treatment of other infections (ie, fluid collection in abdomen, perinephric fluid collection, wound infection, sepsis, drain site infection, peritonitis, and cholangitis).

Infectious complications after stent removal were significantly greater in the preprotocol group than the protocol group (9% vs 3%, $P = .035$; Table 3). Three patients in the preprotocol group had bacteremia, as opposed to none in the protocol group. None of these patients had a preprocedure urine culture within 30 days prior to stent removal. Two patients had *Klebsiella* spp bacteremia and 1 had enterococcal bacteremia. The 2 patients with *Klebsiella* spp bacteremia did not receive any preprocedure antibiotics, and the patient with enterococcal bacteremia received preprocedure cephalexin. There was no difference in acute kidney injury, biopsy-proven rejection, or mortality between the groups. No antibiotic-related adverse effects were identified.

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Table 1. Baseline Demographics and Transplant Characteristics

	Preprotocol (n = 86)	Protocol (n = 151)	P Value
Age, y	56.3 (45.9–64.9)	55.6 (44.2–63.6)	.573
Male	53 (60.2)	99 (65.6)	.408
Duration on dialysis prior to transplant, y	3 (0–6)	4 (1–6)	.271
Race			
African American	47 (53.4)	90 (59.6)	
Caucasian	35 (39.8)	35 (23.2)	
Asian	3 (3.4)	10 (6.6)	
Other	2 (2.3)	11 (7.3)	
Unknown	1 (1.1)	5 (3.3)	
Ethnicity			
Hispanic or Latino	11 (12.5)	24 (15.9)	
Not Hispanic or Latino	76 (86.4)	123 (81.5)	
Unknown	1 (1.1)	4 (2.2)	
Native kidney disease			
Diabetes	31 (35.2)	53 (35.1)	> .999
Hypertension	26 (29.5)	53 (35.1)	.379
Retransplant	12 (13.6)	14 (9.3)	.389
Polycystic kidney disease	6 (6.8)	10 (6.7)	.953
FSGS	6 (6.8)	9 (6.0)	.792
Glomerulonephritis	6 (6.8)	4 (2.6)	.178
Lupus	3 (3.4)	6 (4.0)	> .999
IgAN	2 (2.3)	6 (4.0)	.714
HIVAN	4 (4.5)	1 (0.7)	.063
Alport syndrome	0	2 (1.3)	.533
Congenital obstructive uropathy	1 (1.1)	1 (0.7)	> .999
aHUS	0	1 (0.7)	> .999
TMA	1 (1.1)	0	.368
Vascular	0	1 (0.7)	> .999
Other	8	5	.076
Comorbidities			
Hypertension	80 (90.9)	142 (94.0)	.364
Diabetes	36 (40.9)	63 (41.7)	.902
Active or previous smoker	43 (48.9)	58 (38.4)	.115
COPD	5 (5.7)	6 (4.0)	.539
Induction immunosuppression			
Antithymocyte globulin (rabbit)	57 (63.8)	123 (81.5)	.004
Antithymocyte globulin (rabbit) cumulative dose, mg/kg	5 (4.1–5.5), n = 57	4.8 (3.8–5.4), n = 123	.476
Basiliximab	37 (42.0)	35 (23.2)	.002
Basiliximab cumulative dose, mg	40 (40–40), n = 37	40 (40–40), n = 35	.637
Maintenance immunosuppression at time of stent removal			
Prednisone	87 (98.9)	150 (99.3)	> .999
Prednisone mg/d, mean (SD)	7.7 (4.1), n = 87	10.3 (4.7), n = 150	< .001
Tacrolimus	87 (98.9)	148 (98.0)	> .999
Tacrolimus, mg/d	6 (4–10), n = 87	10 (6–13), n = 148	<.001
Tacrolimus trough, mcg/mL	8.6 (6.8–10.1)	8.5 (6.9–10.65)	.295
Mycophenolate mofetil	76 (86.4)	131 (86.8)	.932
Mycophenolate mofetil mg/d, mean (SD)	1725 (442), n = 76	1492.37 (506), n = 131	.001
Mycophenolic acid	9 (10.2)	18 (11.9)	.690
Mycophenolic acid mg/d	1080 (720–1440), n = 9	720 (720–1440), n = 18	.278
Azathioprine	0	1 (0.7)	> .999
Cyclosporine	1 (1.1)	0	.368
Deceased donor	65 (73.9)	119 (78.8)	.225

Data are presented as median (IQR) or No. (%) unless noted otherwise.

Abbreviations: aHUS, atypical hemolytic uremic syndrome; COPD, chronic obstructive pulmonary disease; FSGS, focal segmental glomerulosclerosis; HIVAN, HIV-associated nephropathy; IgAN, immunoglobulin A nephropathy; TMA, thrombotic microangiopathy.

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Table 2. Stent Removal Characteristics

	Preprotocol (n = 88)	Protocol (n = 151)	P Value
Time to stent removal, d	36 (32–40)	25 (23–31)	< 001
Stent removed while patient was hospitalized	21 (23 9)	32 (21 2)	632
Urinalysis within 30 d prior to stent removal	65 (73 9)	111 (73.5)	302
>20 WBCs	10 (15 4)	8 (7 2)	067
10–20 WBCs	24 (36 9)	52 (46 8)	251
0–5 WBCs	31 (47 7)	51 (45 9)	820
Urine culture within 30 d prior to stent removal	40 (45 5)	141 (94 4)	< 001
Positive urine culture	5 (12 5)	20 (14 2)	080
Organisms growing in most recent urine culture prior to stent removal[a]			
Enterococcus spp	3 (7 5)	8 (5 7)	751
Escherichia coli	1 (2 5)	5 (3 5)	418
Gardnerella vaginalis	0	3 (2 0)	299
Citrobacter spp	1 (2 5)	1 (0 7)	> 999
Klebsiella spp (excluding *K aerogenes*)	1 (2 5)	0	368
Pseudomonas spp	0	1 (0 7)	> 999
Morganella morganii	0	1 (0 7)	> 999
Candida glabrata	0	1 (0 7)	> 999
Other	0	1 (0 7)	> 999
No growth or mixed flora without specific organism identified	35 (87 5)	120 (85 1)	< 001
Received antibiotics preprocedure[a,b]	32 (36.4)	150 (99 3)	< 001
Cephalexin	8 (25 0)	114 (76 0)	< 001
Cefazolin	10 (31.3)	14 (9 3)	604
Ciprofloxacin	6 (18 9)	7 (4 7)	473
Levofloxacin	0	7 (4 7)	049
Cefdinir	0	4 (2.7)	< 001
Cefepime	3 (9 4)	4 (2.7)	710
Amoxicillin	0	4 (2.7)	161
Vancomycin	1 (3 1)	4 (2.7)	654
Tobramycin	0	4 (2.7)	300
Gentamicin	3 (9 4)	2 (1 3)	360
Other[c]	5 (15 6)	7 (4 7)	764
TMP-SMX for prophylaxis at time of stent removal[d]	81 (92 0)	135 (89 4)	651
Received antibiotics postprocedure	10 (11)	29 (19)	148
Duration of antibiotics postprocedure, d	4 (2–15)	4 (2–7)	

Data are presented as median (IQR) or No. (%)

Abbreviations: TMP-SMX, trimethoprim-sulfamethoxazole; WBC, white blood cell

[a]Not mutually exclusive

[b]Does not include TMP-SMX for prophylaxis

[c]Amoxicillin-clavulanate, ampicillin, ceftazidime-avibactam, ceftriaxone, clindamycin, daptomycin, ertapenem, linezolid, meropenem, metronidazole, piperacillin-tazobactam

[d]TMP-SMX dosed at 80–400 mg daily (renally adjusted as needed)

Table 3. Primary and Secondary Outcomes

	Preprotocol (n = 88)	Protocol (n = 151)	P Value
Infectious complications[a]	8 (9.1)	4 (2 6)	.035
UTI	6 (6.8)	4 (2 6)	178
Cystitis	1 (17)	2 (50)	500
Pyelonephritis	5 (83)	2 (50)	.500
Bacteremia	3 (3.4)	0	049
Hospitalization	6 (6.8)	1 (0 7)	011
ED visit without hospitalization	0	1 (0 7)	> 999
Outpatient encounter	5 (5 7)	2 (1 3)	104
Acute kidney injury	16 (18.2)	29 (19.2)	.845
Within 1 y from transplant			
Biopsy-proven rejection	4 (4 5)	7 (4 6)	> 999
Mortality	6 (6 8)	5 (3 3)	220
Antibiotic-related adverse effects	0	0	

Data are presented as No. (%).

Abbreviations: ED, emergency department; UTI, urinary tract infection.

[a]Not mutually exclusive.

Table 4. Multivariate Logistic Regression Assessing Variables Related to Infectious Complications

	Odds Ratio (95% CI)	P Value
Age	1 04 (98–1 11)	202
Retransplant	5 86 (1 14–30 26)	035
Chronic obstructive pulmonary disease	10 06 (1 82–55 71)	008
Prednisone dose	1 18 (1 03–1 35)	014
Protocol intervention	0.18 (05–73)	016

Multivariate logistic regression analysis demonstrated age, history of retransplant, chronic obstructive pulmonary disease (COPD), prednisone dose, and protocol implementation as significantly associated to infectious complications (Table 4). Age, retransplant, COPD, and prednisone dose were associated with an increased risk of infectious complications following stent removal, while protocol intervention was significantly associated with a lower risk of infectious complications (odds ratio, 0.18; 95% CI, 0.05–0.73; $P = .016$) following stent removal. A sensitivity analysis did not find an association between any individual protocol interventions and infectious complications (Supplementary Table 5).

DISCUSSION

After implementing a standardized stent removal protocol, we observed a lower rate of infectious complications within 30 days and no change in immunologic complications within 1 year from transplant. This finding was demonstrated in our primary analysis and supported by multivariate logistic regression analysis. To our knowledge, this study is the first to demonstrate the utility of implementing a standardized stent removal protocol in reducing the incidence of infectious complications and health care utilization.

The AUA guidelines state that antimicrobial prophylaxis may be considered in patients undergoing stent removal, especially when patient and procedural risk factors are present [7]. These recommendations are based on historical studies suggesting

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that antimicrobial prophylaxis at the time of catheter removal may lower the risk of symptomatic UTIs, including 1 small study in renal transplant recipients [10, 11]. The 2019 Infectious Diseases Society of America asymptomatic bacteriuria guideline recommends screening and treating asymptomatic bacteriuria for patients undergoing endoscopic urologic procedures associated with mucosal trauma. However, this does not include cystoscopy with removal of internal ureteric stents [12]. These recommendations are largely based on a meta-analysis evaluating antimicrobial prophylaxis for transurethral prostatic resection, in which bacteriuria and septicemia incidence decreased with the use of antimicrobial prophylaxis [13]. Furthermore, literature comparing the use of antimicrobial prophylaxis vs no prophylaxis in ureteral stent removal in adult kidney transplant recipients has reported no significant differences in the incidence of UTI after stent removal [4, 14, 15]. These results have led many to believe that additional antimicrobial prophylaxis at time of stent removal does not reduce the risk for UTIs. Yet, conflicting data exist, leading to practice variations. A meta-analysis by Antonelli et al found that the median proportion of positive blood cultures was 2% in studies using antimicrobial prophylaxis before stent removal, as compared with 9% in studies without antimicrobial prophylaxis [16]. Among the 20 studies reviewed in the meta-analysis, the average time of stent removal ranged from postoperative days 4 to 25, and the use and choice of antibiotic prophylaxis before stent removal were heterogeneous.

Another key part of the stent removal protocol was the implementation of a more stringent timeline for ureteral stent removal. The 2018 European Association of Urology guidelines on renal transplantation advise centers to remove stents earlier than 6 weeks after transplant; however, there is no consensus regarding the appropriate time of stent removal within those 6 weeks posttransplant [8]. Existing literature has found earlier stent removal, particularly within 3 weeks of placement, to be associated with a decreased incidence of UTIs and no significant difference in incidence of major urologic complications as compared with later removal [4, 5].

In our study, the entire stent removal protocol was associated with a reduced risk of infectious complications. However, neither routine antimicrobial prophylaxis nor early stent removal alone was associated with a reduced risk of infectious complication, and we are unable to ascribe the benefit to any specific aspect of the protocol. Still, it is reasonable to believe that the protocol in its entirety contributed to the improved outcomes associated with the bundled protocol. Unique to our study, the majority of patients were receiving opportunistic infection prophylaxis with TMP-SMX. Additionally, patients received universal culture-directed therapy for antimicrobial prophylaxis for stent removal, and most patients received cephalexin. In contrast, the majority of recipients in the antimicrobial prophylaxis group in the study by Lee et al used fluoroquinolone (75%) and not TMP-SMX prophylaxis (55%) [14]. Notably, our epidemiologic pattern was consistent with that of Lee et al, who had *Enterococcus faecalis* and *E coli* as the 2 most prominent organisms growing in urine cultures following stent removal in kidney transplant patients.

Consistent with previous literature, the multivariate logistic regression analysis found that age, retransplant, COPD, and prednisone were associated with an increased risk of infectious complications. Older kidney transplant recipients have been shown to be at higher risk than younger recipients for infectious complications [17]. Additionally, patients who are exposed to immunosuppression before transplant can have an increased risk of infection—this describes our patients who underwent retransplantion and maintained some degree of immunosuppression following the first transplant. Although the link between COPD and an increased risk of infectious complications is not entirely clear, this association has been described. Inhaled anticholinergic agents, such as ipratropium and tiotropium, have been associated with an increased incidence of acute urinary retention as well as UTIs [18, 19]. Last, higher prednisone dose is an indicator of a higher degree of immunosuppression as compared with lower doses; therefore, the link between prednisone dose and infectious complications can be clearly understood, as patients with a higher degree of immunosuppression are more likely to be at an increased risk for infection [20].

Our study has several limitations. First, our stent removal protocol had multiple components. As a result, we cannot definitively distinguish if any one of these components contributed more to the decreased risk of infectious complications than the others. We performed regression and sensitivity analyses in attempts to mitigate the risk of confounding, although unmeasured confounders could still affect the results. Second, this was a retrospective study, which means that we relied on documentation in the electronic medical record and had to make assumptions when data were missing. For example, we assumed that patients were adherent with antibiotics and that any issues with adherence would be documented. Yet, this limitation of inaccurate documentation would have affected both groups, and the urology division asked patients about antibiotic compliance prior to stent removal. We also did not have preprocedure urine cultures for everyone in the preprotocol group, and we assumed that patients who did not have a urine culture did not have preprocedure bacteriuria. Third, this was a single-center study, and differences in patient and transplant characteristics may limit the external validity of our study. Microbiologic epidemiology and antimicrobial resistance patterns may differ as well, and other centers may not achieve the same results. Furthermore, most of our patients received TMP-SMX for opportunistic infection prophylaxis, and other transplant centers may have different stent removal timelines posttransplant. In centers that already remove stents within 3 weeks posttransplant, this type of intervention may not be as effective.

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Fourth, given the quasi-experimental study design, there were several differences between the groups in our study. More patients in the protocol arm received antithymocyte globulin (rabbit) than the preprotocol group. Our institution has shifted to prefer antithymocyte globulin (rabbit) over time, which explains why more patients in the protocol group received it than the preprotocol group. Additionally, our institution was using more basiliximab during the height of the COVID-19 pandemic, due to fear of complete T-cell depletion with antithymocyte globulin (rabbit). The exposure to increased immunosuppression in the protocol group should have theoretically resulted in an increase in infectious complications; however, despite more antithymocyte globulin (rabbit) use, protocol implementation decreased infectious outcomes after urinary stent removal.

Fifth, our reliance on a culture to define a UTI may undercall UTIs if patients were unable to obtain a culture, particularly in the outpatient setting. However, this definition is consistent with the 2019 guideline on UTI in solid organ transplant recipients from the American Society of Transplantation Infectious Diseases community of practice, which describes a UTI as the growth of a uropathogen in the urine and the necessity of symptoms [21]. To account for this potential limitation, we included patients with a "possible UTI" as part of our composite end point if they had a hospitalization, emergency department visit, or outpatient encounter. Reliance on nephrologists to diagnose UTIs may influence the results, although this reflects real-world practice, as routinely screening for asymptomatic bacteriuria posttransplant is not recommended [12].

Sixth, protocol deviation was observed in 39 patients (16%) who continued antibiotics after stent removal. However, since the median duration of antibiotics postprocedure was the same between the groups, we believe that this is unlikely to have biased the efficacy of the results. Finally, we were unable to capture data to evaluate the potential long-term implications on antimicrobial resistance, if antimicrobial prophylaxis is routinely used. Our study was not designed to evaluate the impact of prescribing antimicrobial prophylaxis only to patients with preprocedure bacteriuria.

CONCLUSION

Ureteral stenting and direct manipulation of the ureter during stent removal increase the risk of infectious complications in renal transplant recipients [2, 3, 8, 14, 15]. Existing literature is limited on best practices to reduce infectious complications associated with ureteral stent removal, leading to practice variations [21, 22]. Our study demonstrated that the implementation of a standardized stent removal protocol—including obtaining a preprocedure urine culture, prescribing universal culture-directed antimicrobial prophylaxis, and targeting stent removal at 3 weeks posttransplant—was associated with a reduction in infectious complications.

While routine screening for bacteriuria and antibiotic prophylaxis in this setting are controversial, antimicrobial stewardship principals promote the appropriate use of antimicrobials to improve patient outcomes. Our results demonstrate the benefits of a standardized stent removal protocol on reducing the rate of infectious complications and subsequent health care utilization and costs. Future directions include evaluating the impact of each protocol component on the rate of infectious complications, including prescribing antimicrobial prophylaxis only to patients with preprocedure bacteriuria.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Acknowledgments. We have no financial interests with commercial entities that may have a direct interest in the subject matter of this study. We acknowledge Ken Pursell and all others involved in the implementation and maintenance of this protocol.

Potential conflicts of interest. All authors: No reported conflicts.

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ARTICLE

Early Removal of Ureteral Stent After Kidney Transplant Could Decrease Incidence of Urinary Tract Infection: A Systematic Review and Meta-Analysis

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Abstract

Objectives: **In this systematic review and meta-analysis, our aim was to explore the optimal timing of ureteric stent removal after kidney transplant.**
Materials and Methods: **For our analyses, we searched the Cochrane Central Register of Controlled Trials, PubMed, and Embase databases for all randomized clinical trials that evaluated the timing of stent removal after kidney transplant. Patients with early versus late stent removal were compared.**
Results: **Seven eligible studies published from 2012 to 2018, which included 1277 patients, were found to be within the scope of our study. Significant differences were shown between early versus late stent removal groups with regard to development of urinary tract infections (relative risk of 0.42; 95% CI, 0.26-0.685; $P < .001$). In a further subgroup analysis of incidence of urinary tract infection with consideration of heterogeneity, early stent removal was also favored (relative risk at 2 and 3 weeks of 0.36 and 0.35, respectively; $P < .001$ for both). However, with regard to incidence of major urologic complications, there were no significant differences between early and late stent removal (odds ratio at 2 and 3 weeks of 2.79 and 1.97, respectively; $P = .18$ and $P = .26$, respectively). There were also no significant differences between groups in risk of development of urinary leakage (odds ratio at 2 weeks of 3.02, $P = .18$; and relative risk at 3 weeks of 2.00, $P = .27$). With regard to ureteral stenosis, only 3 cases were reported in the late stent removal group.**
Conclusions: **Our study demonstrated that early ureteral stent removal (that is, not later than 3 weeks) could significantly decrease the incidence of urinary tract infections without affecting incidence of major urological complications. We suggest that the appropriate timing of stent removal should be within 14 to 21 days.**

Key words: *Ureteral stenosis, Urinary leakage, Urologic complications*

Introduction

Over the decades, most surgical techniques involved in kidney transplant (KTx) have been standardized. The double J stent (JJ stent)[1,2] has been mostly used in draining after ureteroneocystostomy of KTx, and previous studies have demonstrated that it can decrease the incidence of major urologic complications (MUCs), that is, both ureteric obstruction and ureteric leakage, from between 7% and 9% to 1.5%. However, according to the KTx transplant guidelines from the European Association of Urology,[3] JJ stents can also increase the risk of urinary tract infections (UTIs) from 6% to 40% if left in place for longer than 30 days. The guidelines also advise centers to remove stents earlier than 6 weeks after transplant rather than later. Thus, the ureteric stent is similar to a double-edged sword for KTx recipients: it is helpful in the prevention of MUCs[4] but is a high-risk factor in the development of UTIs[5] and idiosyncratic complications such as hematuria and irritative bladder symptoms.[6] Appropriate application of the ureteric stent is important in KTx.

There are different opinions among surgeons with regard to timing for stent removal. Some researchers[7,8] have asserted that KTx recipients could only benefit from stents placed for 1 or 2 weeks; however, other researchers[9,10] have suggested that indwelling stents can only prevent complications if left for longer periods of time, with too early removal of stents associated with UTIs as well as ureteric leakage. So far, no consensus on the appropriate time of stent removal has been reached.

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Acknowledgements: The authors have not received any funding or grants in support of the presented research or for the preparation of this work and have no declarations of potential conflicts of interest.
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Experimental and Clinical Transplantation (2022) 1: 28-34

DOI: 10.6002/ect.2021.0183

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In this meta-analysis and systematic review, we aimed to identify the optimal "early" timing of ureteric stent removal after KTx, which could be helpful for clinical decisions among transplant centers.

Materials and Methods

Selection criteria

All studies included in our analyses were published in English and conformed to the following criteria: (1) studies on KTx patients, but not those on stenting of ileal conduits or continent urinary diversions, who had urinary stent removal posttransplant; (2) studies designed as randomized controlled trials (RCTs); and (3) studies that included at least 1 outcome. Duplicated results in different articles, reviews, and animal research studies were excluded.

Search strategy

With use of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and above selection criteria, we searched PubMed, Embase, and the Cochrane Library databases for studies published from February 2011 to October 2019. Potentially relevant RCTs from references of relative studies were also searched by hand to ensure that no articles were missed. The followed medical subject headings (MeSH) or non-MeSH terms were used in our search: "kidney graft" OR "kidney transplantation" OR "renal transplant" OR "kidney transplant" AND "stent" and "urinary stent." These search strategies were used to search each database.

Outcome measures

The outcome measure in this meta-analysis was the timing of stent removal and the incidence of UTIs and MUCs (urinary leakage and ureteral stenosis).[11] Urinary tract infections were defined as a positive urine culture with a bacterial colony count of more than 10^5 colony-forming units/mL.[12]

Data extraction

Two reviewers independently assessed all eligible publications, and any disagreements were discussed with a third reviewer and solved by all reviewers. With selection criteria, each reviewer used a standardized extraction form to extract the data from all full-text studies, which included details on author names, the year of publication, country, general patient data, follow-up duration, donor type, type of stent, stent removal methods, immunosuppressive therapies, and outcomes.

Statistical analyses

Review Manager Software (RevMan 5.3) was used for meta-analysis. Differences in outcomes were expressed as relative risk (RR) or odds ratio (OR; with 95% CIs). Heterogeneity across trials was quantified by using the I^2 statistic. When I^2 statistic was below 50% by chi-square test, which indicted a low level of heterogeneity, a fixed-effects model was used for estimates. When I^2 statistic was over 50%, a random-effects model was chosen. Furthermore, subgroup analysis was used to explore possible sources of heterogeneity, and sensitivity analyses were performed to examine the results. $P < .05$ was affirmed as statistically significant.

Quality assessment

The GRADE tool[13,14] was recommended for assessing the risk of bias and evaluating the methodological quality of each RCT, which included 7 aspects: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other biases. Each reviewer assessed each study to find high, low, or unclear risk of bias. Disagreements were resolved through a third reviewer and discussion.

Results

After careful review of the initial literature search, a total of 7 eligible studies[15-21] from 2012 to 2018 and 1277 patients were found to be within the scope of our study. Figure 1 illustrates the selection strategy, and Table 1 lists the characteristics of the 7 included studies. Figure 2 illustrates the quality assessment of each RCT and provides a qualification of risk of bias. All studies except Parapiboon and colleagues[18] reported the age of the recipients. Five of the 7 articles reported the use of the Lich-Gregoir technique, which was not reported in the remaining 2 studies. Regarding stent removal, cystoscopy was mostly used in the studies. Six studies recorded the use of antibiotic prophylaxis, such as ceftriaxone and sulfamethoxazole/trimethoprim, to protect or to prevent UTIs. Five studies reported the immunosuppressive therapies that patients received. With regard to outcomes, all articles described the incidence of UTIs and 4 articles reported MUCs. Table 2 presents the outcomes for the included studies.

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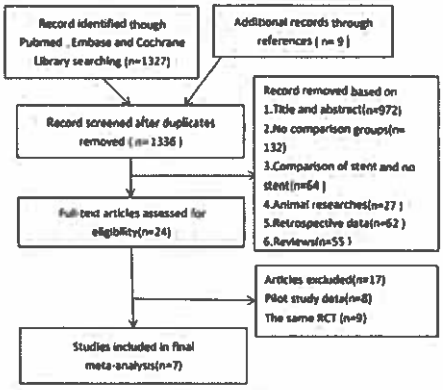
Table 1. Characteristics of 7 Included Randomized Controlled Trials

Study	Year	Timing of Stent Removal	No. of Patients	Mean Patient Age	Follow Up	Type of Stent	LD/DD, %	UNC Technique	Technique of Stent Removal	IS Therapy	Prophylactic Antibiotics
Huang et al[16]	2012	<3 weeks >6 weeks	179 186	42.8 y 43.5 y	3 months	JJ stent	0%/100%	Lich-Gregoir	Cystoscopy	CNI + MMF + Pred	Yes
Indu et al[17]	2012	<7 days >28 days	50 50	34.4 y 33.8 y	6 months	JJ stent	100%/0%	Lich-Gregoir	NR	Cyc + Aza/ MMF + Pred	Yes
Parapiboon et al[18]	2012	7-14 day >14 days	37 37	NR	2 months	NR	58.10%	Lich-Gregoir	Cystoscopy	Cyc + Tac + MMF + Cor	Yes
Gunawansa et al[21]	2014	<6 days >28 days	203 179	NR	16 months	NR	NR	NR	Attached to UC Cystoscopy	NR	NR
Liu et al[20]	2016	<7 days	52	34.9 y	3 months	JJ stent	100%/0%	Lich-Gregoir	Attached to UC Cystoscopy	CNI + MMF + Cor + Bas	Yes
Patel et al[19]	2017	<5 days >6 weeks	79 126	47.5 y 41.7 y	3 months 6 months	JJ stent	60.5%/39.5% 65.6%/34.4%	Lich-Gregoir	Attached to UC Cystoscopy	NR	Yes
Appiya et al[15]	2018	<14 days	24	30.8 y	6 months	JJ stent	NR	NR	Cystoscopy	Tac + MMF + Pred	Yes

Abbreviations: Aza, azathioprine; Bas, basiliximab; CNI, calcineurin inhibitors; Cor, corticosteroids; Cyc, cyclosporine; Dac, Daclizumab; DD, deceased donor; IS, immunosuppression; JJ stent, double J stent; LD, living donor; LG, Lich-Gregoir; MMF, mycophenolate mofetil; NR, not reported; Pred, prednisone; Tac, tacrolimus; UC, urinary catheter; UNC, ureteroneocystostomy; y, year

Figure 1. Flowchart of Included Studies in the Meta-Analysis

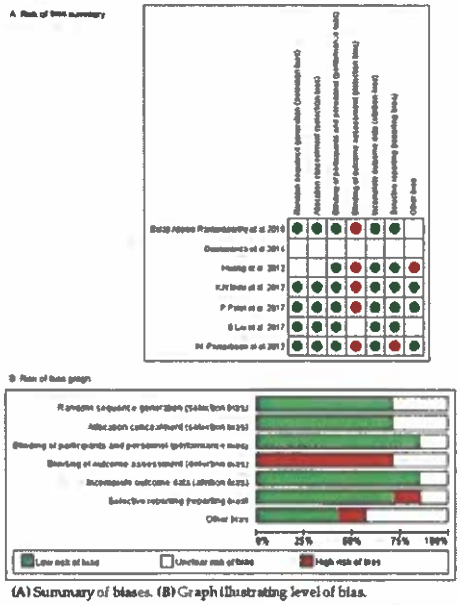


Abbreviations: RCT, randomized controlled trial

Urinary tract infections

All included studies recorded UTI events with regard to various timing of stent removal. Significant differences were shown between groups with early versus late stent removal in the development of UTIs, with early removal shown to have better outcomes for UTI incidence (RR of 0.42; 95% CI, 0.26-0.685; $P < .001$) (Figure 3A). With the consideration of high heterogeneity (I^2 = 56%), sensitivity analysis and subgroup analysis were conducted. To explore appropriate timing, we investigated 2 timelines: 2 weeks and 3 weeks. To avoid low quality and high risk of bias, we excluded Gunawansa and associates[21] (the full article was not assessable). This article was also excluded for our continuous analysis of MUC. Our analysis was consistent with the previous conclusion without heterogeneity, which favored early stent removal. At the 2-week timeline, relative risk was 0.36 (95% CI, 0.26-0.52; $P < .001$; Figure 3B); at the 3-week timeline, relative risk was 0.35 (95% CI, 0.25-0.49; $P < .001$; Figure 3C).

Figure 2. Qualification of Risk of Bias



(A) Summary of biases. (B) Graph illustrating level of bias.

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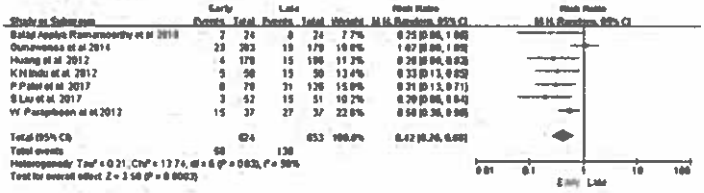
Table 2. Outcomes Shown in the 7 Included Randomized Controlled Trials

Study	Year	Timing of Stent Removal	Total No. of Patients	No. of Complications				UTI, %	MUC, %	Urinary Leakage, %	Ureteral Stenosis, %
				UTI	MUC	Urinary Leakage	Ureteral Stenosis				
Huang et al[16]	2012	<3 weeks	179	4	2	2	0	2.2%	1.10%	1.10%	0%
		>6 weeks	186	15	2	2	0	8.1%	1.10%	1.10%	0%
Indu et al[17]	2012	<7 days	50	5	1	1	0	10.0%	2.00%	2.00%	0%
		>28 days	50	15	0	0	0	30.0%	0%	0%	0%
Parapiboon et al[18]	2012	7-14 day	37	15	NR			40.50%	NR	NR	NR
		>14 days	37	27				72.90%			
Gunawansa et al[21]	2014	<6 days	203	23	0	0	0	11.30%	0%	0	0%
		>28 days	179	19	2	0	2	10.60%	1.10%	0	1.10%
Liu et al[20]	2016	<7 days	52	3	0	0	0	5.8%	0%	0%	0%
		>28 days	51	15	0	0	0	29.4%	0%	0%	0%
Patel et al[19]	2017	<5 days	79	6	3	2	1	7.6%	3.70%	2.50%	1.20%
		>6 weeks	126	31	1	0	1	24.6%	0.80%	0%	0.80%
Appiya et al[15]	2018	<14 days	24	2	1	1	0	8.30%	4.20%	4.20%	0%
		>6 weeks	24	8	1	1	0	33.30%	4.20%	4.20%	0%

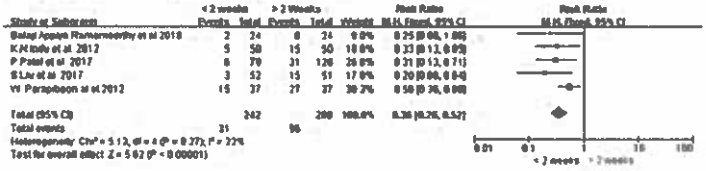
Abbreviations: NR, not reported

Figure 3. Meta-Analysis of Urinary Tract Infection

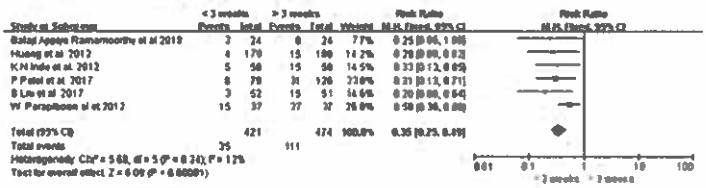
A. UTI (Early or late).



B. UTI -subgroup (< 2 weeks or > 2 weeks).



C. UTI -subgroup (< 3 weeks or > 3 weeks).



Abbreviations: M-H, Mantel-Haenszel; UTI, urinary tract infection

Major urological complications

Four studies described the incidence of MUCs with a total of 718 patient. As shown in Figure 4, with regard to MUCs, there were no significant differences among the studies between early and late stent removal. The OR for 2-week timeline was 2.79 (95% CI, 0.62-12.52; $P = .18$), and the OR for 3-week timeline was 1.97 (95% CI, 0.61-6.33; $P = .26$). As shown in Figure 5, we also observed no significant differences between early and late stent removal groups in risk of developing urinary leakage, with OR for 2-week timeline of 3.02 (95% CI, 0.59-15.51;

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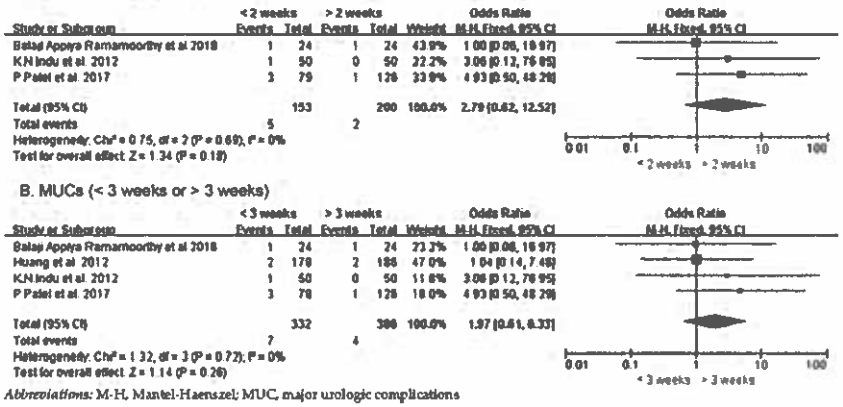
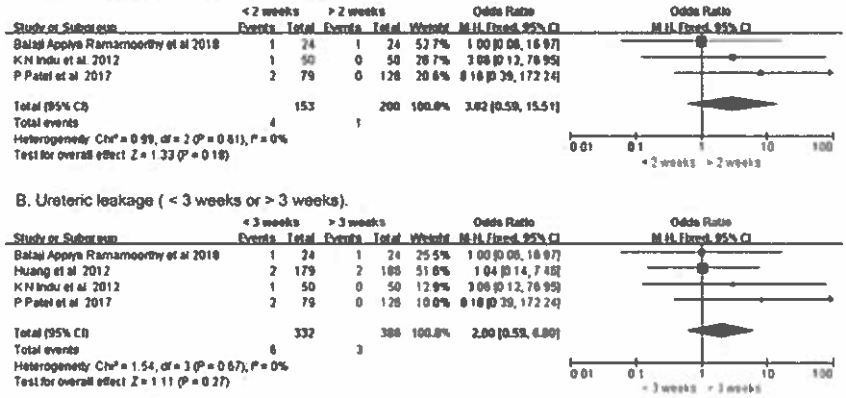
Figure 4. Meta-Analysis of Major Urologic Complications



Abbreviations: M-H, Mantel-Haenszel; MUC, major urologic complications

Figure 5. Meta-Analysis of Ureteric Leakage



Abbreviations: M-H, Mantel-Haenszel

P = .18) and RR for 3-week timeline of 2.00 (95% CI, 0.59-6.80; P = .27). For ureteral stenosis, only Gunawansa and colleagues[21] (2 cases) and Patel and colleagues[19] (1 case) reported ureteral stenosis, all at late stent removal. Therefore, because of the low incidence among our findings, this factor was not suitable for the meta-analysis.

Discussion

The universal use of ureteric stents is a good minimally invasive option for urinary drainage after KTx; however, there are still questions on indwelling time. Previous research[5] has shown that the implanted stent can be accompanied by various complications, including hematuresis, stent migration, and discomfort. In addition, it may lead to UTIs, which could result in prolonged hospitalizations, increased costs, and even recurrent surgical interventions. However, the benefits of stents have also been shown, with KTx recipients having a lower incidence of MUCs. A number of studies[22-24] have explored timing of stent removal after KTx, with ureteral stent removal usually occurring from 1 to 6 weeks after the surgery.

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Because, so far, no consensus has been reached with regard to timing, we explored this aspect with a systematic review and meta-analysis.

In our analysis, we found that early removal of the stent after KTx (that is, not later than 3 weeks) had a significant effect on decreasing the incidence of UTIs. We found that timing at both 2 weeks and 3 weeks had good results; therefore, we suggest 14 to 21 days as a preferred timing. In their study, Yuksel and colleagues[10] reviewed 818 KTx patients and divided them into 4 groups according to the timing of stent removal (5-7 days, 8-14 days, 15-21 days, >22 days). They found that only 0.1% of UTIs were observed at 15 to 21 days versus 1.2% at 8 to 14 days and 3.2% at >22 days, with obvious lower incidence among those who had JJ stent removal before day 14 (10.6% in the combined group of 5-7 days and 8-14 days). Dadkhah and colleagues[9] also showed a lower rate of UTIs in patients who had stent removal at about 20 days versus those who had removal at about 30 days after KTx (7.2% vs 12.4%, respectively). These results imply that long-duration indwelling stents could lead to high risk of UTIs.

In contrast to the results for UTIs, our analysis showed that development of MUCs was not associated with indwelling time of stents. We also found no significant differences between groups with short and long duration of stent placement with regard to risk of developing urinary leakage, with negligible rate of ureteral stenosis (0.6%). As reported previously,[25-28] the incidence of urinary leakage can range from 1.5% to 6.0%, with most leakages occurring at the site of the ureteroneocystostomy during the early stage due to distal ureteral ischemia. In a meta-analysis from Alberts and colleagues,[29] several factors, including graft arterial reconstruction, recipient diabetes, and multiple renal arteries, were concluded to contribute to ureteral leakage after KTx, with the Lich-Gregoir technique suggested to significantly reduce the rate of leakage. Furthermore, Yuksel and colleagues[10] reported that early stent removal (<14 days) led to a higher rate of leakage and stenosis than in the unstented population. Thus, we suggest that more than 2 weeks of the implanted stent could help to prevent leakage, but longer indwelling time may have no effect on the incidence of ureteral leakages after KTx. With these considerations, we recommend removal of the ureteral stent after 2 weeks.

This meta-analysis also carries some limitations that must be considered. First, only 7 RCTs were included in our study, and 1 of the studies carried a high risk of bias, resulting in our minimization or exclusion of those results for some analyses. Second, each RCT contained a small numbers of patients; therefore, larger RCTs may be needed to confirm these results. In addition, only studies written in English were searched in this meta-analysis, which resulted in potential publication bias. Finally, various recipient and donor characteristics of included studies could also have affected our results. Because of these limitations, more trials may be needed to confirm these results.

Conclusions

Our study demonstrated that the early removal of ureteral stent, not later than 3 weeks, significantly decreased the incidence of UTI but did not affect the development of MUCs. We recommend that stent placement of 14 to 21 days is a preferred duration and the appropriate timing of stent removal.

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frontiers in Oncology

REVIEW
published: 06 September 2016
doi: 10.3389/fonc.2016.00201

The Place of FDG PET/CT in Renal Cell Carcinoma: Value and Limitations

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Unlike for most other malignancies, application of FDG PET/CT is limited for renal cell carcinoma (RCC), mainly due to physiological excretion of 18F-fluoro-2-deoxy-2-D-glucose (FDG) from the kidneys, which decreases contrast between renal lesions and normal tissue, and may obscure or mask the lesions of the kidneys. Published clinical observations were discordant regarding the role of FDG PET/CT in diagnosing and staging RCC, and FDG PET/CT is not recommended for this purpose based on current national and international guidelines. However, quantitative FDG PET/CT imaging may facilitate the prediction of the degree of tumor differentiation and allows for prognosis of the disease. FDG PET/CT has potency as an imaging biomarker to provide useful information about patient's survival. FDG PET/CT can be effectively used for postoperative surveillance and restaging with high sensitivity, specificity, and accuracy, as early diagnosis of recurrent/metastatic disease can drastically affect therapeutic decision and alter outcome of patients. FDG uptake is helpful for differentiating benign or bland emboli from tumor thrombosis in RCC patients. FDG PET/CT also has higher sensitivity and accuracy when compared with bone scan to detect RCC metastasis to the bone. FDG PET/CT can play a strong clinical role in the management of recurrent and metastatic RCC. In monitoring the efficacy of new target therapy such as tyrosine kinase inhibitors (TKIs) treatment for advanced RCC, FDG PET/CT has been increasingly used to assess the therapeutic efficacy, and change in FDG uptake is a strong indicator of biological response to TKI.

Keywords: renal cell carcinoma, FDG PET/CT, staging, restaging, tyrosine kinase inhibitors

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Edited by:
Georgios S. Limouris, National and Kapodistrian University of Athens, Greece

Reviewed by:
Nghi Co Nguyen, University of Pittsburgh, USA
Cigdem Soydal, Ankara University, Turkey

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Specialty section:
This article was submitted to Cancer Imaging and Diagnosis, a section of the journal Frontiers in Oncology

Received: *29 February 2016*
Accepted: *26 August 2016*
Published: *06 September 2016*

Citation:
Liu Y (2016) The Place of FDG PET/CT in Renal Cell Carcinoma: Value and Limitations. Front. Oncol. 6:201. doi: 10.3389/fonc.2016.00201

INTRODUCTION

Renal cell carcinoma (RCC) is the most common solid tumor of the kidneys, accounting for 3% of all malignancies and representing the seventh leading cause of cancer. The most common histological subtype of RCC is clear cell RCC, followed by papillary carcinoma. Standard imaging evaluation for the characterization of primary renal tumor includes ultrasound, CT, and MRI. Cross-sectional imaging, especially contrast CT, is a primary imaging modality for tumor detection and diagnosis, and its increasing use has led to an increased diagnosis of RCC. Surgical resection through either partial or radical nephrectomy remains the mainstay of treatment for the localized disease.

Positron emission tomography (PET) has emerged as one of the most important imaging modality in staging, restaging, detecting recurrence and/or metastasis, and monitoring therapeutic response in most malignant diseases (1, 2). In PET, a trace amount of a radioactive compound is administered, and the resultant images are obtained from three-dimensional spatial reconstructions. The intensity of the imaging signal is proportional to the amount of tracer and, therefore, is potentially

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semiquantitative (3). Whereas conventional imaging techniques can provide information on anatomic abnormalities, PET imaging relies on both molecular biology and *in vivo* imaging to provide information about the preceding changes in metabolism and function, including glucose metabolism, cell proliferation, cell membrane metabolism, or receptor expression. Furthermore, integrated PET/CT units allow correct co-registration and fused imaging of anatomical and functional data. The integration of CT imaging with PET has been demonstrated to significantly decrease false positive results and improve accuracy of the PET study (4–6).

18F-fluoro-2-deoxy-2-D-glucose (FDG), a non-physiological radiotracer with a chemical structure similar to that of naturally occurring glucose, is most commonly used in PET imaging. FDG enters cells through the same membrane glucose transporter proteins utilized by glucose, which are commonly overexpressed in cancer cells (7, 8). FDG imaging relies upon Warburg's observation that increased glycolysis generated adenosine triphosphate is required to meet the metabolic demands of rapidly dividing tumor cells. Membrane glucose transporters, mainly GLUT-1, actively transport FDG into the cell, where hexokinase then converts it into FDG-6-phosphate. As FDG-6-phosphate is not a substrate for further steps in glycolysis, it is trapped in the cell and accumulates correspondingly to the cell's glucose metabolic activity. FDG accumulation rate is semiquantitatively measured by the standardized uptake value (SUV). Malignant cells exhibit increased FDG accumulation due to increased membrane transporters, increased intracellular hexokinase, and low glucose-6-phosphatase (8).

Unlike for most other malignancies, application of FDG PET/CT is limited for RCC, mainly due to physiological excretion of FDG from the kidneys, which decreases contrast between renal lesions and normal tissue, and may obscure or mask the lesions of the kidneys. However, published clinical observations were discordant. In the era of PET/CT in oncology, clarification and validation of FDG PET/CT for RCC is of great significance for urologists, oncologists, and radiologists. This review presents the studies regarding the FDG PET/CT for RCC. The role of FDG PET/CT is discussed based on the critical, non-structured review of the literature.

FDG PET/CT FOR PRIMARY RCC

Many early clinical observations showed unfavorable results about the role of FDG PET/CT for detection and characterization of lesions of the kidney, with pooled sensitivity of 50–60% (9). Even forced diuresis coupled with parenteral hydration could not improve the sensitivity (10). In Miyakita's study (11), 19 consecutive patients with RCC were imaged using FDG PET preoperatively, the results of which were then compared with the histology obtained after radical surgery. Increased FDG uptake was found in only in 6 out of the 19 patients (31.5%) while immunohistochemistry of GLUT-1 in RCC produced varying results; there was no correlation of GLUT-1 immunoreactivity and FDG PET positivity. Aide et al. prospectively compared the efficiency of FDG PET with diagnostic CT in the characterization and primary staging of 35 suspicious renal masses (12). A high rate of false negative results was reported with FDG PET, leading to 47% sensitivity, 80% specificity, and 51% accuracy; all lower than those of CT. The author concluded that, in the characterization of renal masses, FDG PET imaging does not offer any additional advantages compared with CT. In another retrospective study of 66 patients with known RCC by Kang et al. (13), the accuracies of FDG PET and conventional imaging modalities were also compared. FDG PET exhibited a sensitivity of 60% and specificity of 100% for primary RCC tumors, while abdominal CT demonstrated 91.7% sensitivity and 100% specificity. Ozulker et al. evaluated the efficacy of FDG PET/CT in the detection of RCC in patients with indeterminate renal masses detected by conventional imaging from 18 patients (14). All patients underwent nephrectomy or surgical resection of the renal mass, and the final diagnoses were based on histopathology. Fifteen patients had RCC, and three renal tumors were benign. FDG PET/CT accurately detected seven malignant lesions and false negative results in eight patients. FDG PET/CT yielded true negatives in two cases of renal cortical cyst and false positive in one case with oncocytoma. For primary RCC tumors, PET showed 46.6% sensitivity, 66.6% specificity, and 50% accuracy. The median size of visualized tumors was greater than that of non-visualized tumors, and the average Fuhrman grade of the patients with FDG-positive malignant lesions were higher than that of the patients with FDG-negative lesions. There was no significant change in average and maximum SUVs between early and delayed imaging for malignant tumors.

However, some clinical observations demonstrated favorable results regarding the role FDG PET/CT in RCC and showed high FDG avidity in the majority of RCC lesions. In a study by Kumar et al. (15), FDG PET was performed in 28 solid renal masses visualized by CT/MRI. Of the lesions, FDG PET was accurately able to depict 23 out of 27 (85%) malignant renal masses. Of the 10 primary renal tumors (9 malignant, 1 benign), FDG PET yielded 8 out of 9 true positive results (89%), 1 true negative, and 1 false negative. In addition to characterization of the lesions, FDG PET also contributed to primary staging, altering management in 3 out of 10 patients (30%). Of metastatic renal tumors, FDG PET was positive in 15 out of 18 (83%). There was no significant difference in SUVs between primary and metastatic renal masses. Nakhoda et al. evaluated the sensitivity of FDG PET/CT to detect different renal lesions (16). Fifteen out of 18 RCC were detectable by PET, whereas all renal lymphomas and metastases were detectable. None of the metabolic parameters were statistically significant between RCC and renal lymphoma. However, all metabolic parameters were statistically and significantly greater for renal metastases compared with RCC and renal lymphoma, and for clear cell RCC compared with papillary RCC. In addition to a sensitivity of 88% for detection of solid malignant renal lesions in patients with known renal malignancy, FDG PET/CT also reveals differences in metabolic activity based on histopathological type.

Recently, Takahashi et al. retrospectively analyzed FDG PET/CT findings in 98 lesions from 93 patients who had partial or radical nephrectomy after imaging (17). The SUVs of high-grade clear cell RCC were significantly higher when compared with that of the control benign lesions and low-grade tumors. An optimal SUV cutoff value of 3.0 had 89% sensitivity and 87% specificity

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in differentiating between high-grade and low-grade clear cell RCCs. Multiple regression analysis demonstrated that a high-grade clear cell RCC was the most significant predictor of SUV.

Overall, the results were heterogeneous. Although FDG PET/CT may be helpful in the characterization and detection of primary renal tumors, it has low negative predictive value. In addition, it seems that FDG PET/CT does not have significant advantage in diagnosis and staging of RCC compared with the diagnostic CT.

PREDICTIVE ROLE OF FDG PET/CT IN PROGNOSIS

Metabolic quantitation by SUV measurement on FDG PET/CT may play a role in the evaluation of biological behavior of lesion and prediction of patient's prognosis. Namura et al. evaluated the impact of the maximum SUV (SUV_{max}) from FDG PET/CT on survival in 26 patients with advanced RCC (18). High SUV_{max} in patients with RCC correlated with poor prognosis, as there was a statistically significant difference in the survival between patients with SUV_{max} equal or greater than the mean of SUV_{max}, 8.8 and patients with SUV_{max} less than 8.8. The authors revealed that the SUV_{max} might have a role as a novel biomarker in prognosticating the survival time of patients with advanced RCC by multivariate analyses with standard risk factors or risk classifications. In another study by Ferda et al. (19), 60 RCC patients had follow-ups for development of the disease 12 months after FDG PET/CT. The highest FDG accumulation was seen in the tumor of the highest grade, and the highest mortality was found for tumors exceeding SUV_{max} of 10. Lee et al. investigated the relationship between the SUV_{max} of primary RCC with and without metastatic lesions in 23 patients (20). The median SUV_{max} of primary RCC of the 16 patients without metastasis was 2.6 (range of 1.1–5.6) while that of the patients with metastasis was 5.0 (range of 2.9–7.6). The SUV_{max} of the primary RCC with metastasis (5.3 ± 1.7) was significantly higher than those without metastasis (2.9 ± 1.0). Thus, one of the roles of FDG PET/CT in the initial evaluation of a patient with RCC may be in predicting extrarenal disease, as patients who have primary RCC with high SUV_{max} are suggested to have a likelihood of metastasis.

Based on the limited data, quantitative FDG PET/CT imaging may facilitate the prediction of the degree of tumor differentiation and allow for prognosis of the disease. FDG PET/CT may be an effective imaging biomarker to provide useful information about patient's survival. However, more studies are needed to justify these preliminary findings.

FDG PET/CT FOR RESTAGING RCC

Metastatic RCC is one of the most lethal urologic cancers. Up to one-third of patients with newly diagnosed RCC have metastatic diseases (21). Even after nephrectomy of a locally confined disease, more than 30% of the patients develop metastases, most commonly to the lung, bone, skin, liver, and brain (21). Effective staging of RCC, therefore, is crucial for the management of patients.

Although the role of FDG PET/CT in diagnosing RCC is conflicting, it has been more effective in the detection of metastatic disease, thus affecting therapeutic decisions. Obviously, size of the lesions has been shown to be a significant factor affecting sensitivity of PET/CT. Majhail et al. evaluated the performance of FDG PET in detecting metastatic lesions in 24 patients with histologically proven RCC and suspected distant metastases based on conventional anatomic imaging (22). Histologically documented distant metastases were present in 33 sites. Overall sensitivity, specificity, and positive predictive value of FDG PET for the detection of distant metastases from RCC was 63.6% (21 out of 33), 100% (3 out of 3), and 100% (21 out of 21), respectively. The mean size of distant metastases in patients with true positive FDG PET was 2.2 cm (95% CI, 1.7–2.6 cm) compared with 1.0 cm in patients with false negative FDG PET.

18F-fluoro-2-deoxy-2-D-glucose (FDG) PET seems useful for postoperative surveillance in patients with RCC. It can detect recurrence in the surgical site. Nakatani et al. evaluated the surveillance role of FDG PET in 23 postoperative patients with RCC (23). Histological final diagnosis of at least 6 months clinical follow-up was used to confirm diagnostic accuracy of visually interpreted PET. FDG PET was demonstrated to have 81% sensitivity, 71% specificity, and 79% diagnostic accuracy. PET was able to accurately detect local recurrence and metastases to the peritoneum, bone, muscle, and adrenal gland in all cases. In six cases (21%), additional information was obtained from scans, ultimately affecting the course of therapeutic management in three cases (11%). The cumulative survival rate over 5 years in the PET-positive was 46%, whereas that of the PET-negative group was 83%. Kumar et al. assessed 103 FDG PET/CT scans of 63 patients with suspected recurrent RCC after nephrectomy, confirmed with histological examination and/or clinical follow-up and conventional imaging modalities (24). The results of the 103 FDG PET/CT scans were 63 true positive studies, 30 true negative studies, 7 false negative studies, and 3 false positive studies. 109 lesions were detected by FDG PET/CT in the 63 true positive scans. FDG PET/CT was demonstrated to have 90% sensitivity, 91% specificity, and 90% accuracy in the study. Bertagna et al. retrospectively evaluated 68 patients with renal carcinoma who had postoperative FDG PET/CT following partial or radical nephrectomy (25). FDG PET/CT was reported to have 82% sensitivity, 100% specificity, 100% positive predictive value, 66.7% negative predictive value, and 86.6% accuracy. In another study reported by Fuccio et al., the usefulness of FDG PET/CT was assessed in the restaging of 69 RCC patients with clinical or radiological suspicion of metastases after nephrectomy (26). Validation of FDG PET/CT results was established by biopsy, other imaging modalities, and/or clinical and radiological follow-up of 12 months. Forty patients had true positive, 2 patients false positive, 23 patients true negative, and 4 patients false negative. Sensitivity, specificity, accuracy, positive predictive value, and negative predictive value were 90, 92, 91, 95, and 85%, respectively. On a lesion basis, FDG PET/CT detected 114 areas of abnormal uptake in 42 positive patients of which 112 resulted to be true positive.

In another large series study, Win and Aparici retrospectively reviewed the FDG PET/CT studies in 315 RCC patients with biopsy results (27). FDG PET/CT studies exhibited 100%

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sensitivity and 100% specificity in detecting all metastatic lesions of RCC, the smallest of which detected was a 7 mm lymph node. Therefore, the authors recommended the use of FDG PET/CT in routine standard protocols for RCC.

18F-fluoro-2-deoxy-2-D-glucose (FDG) PET/CT is a valuable tool both in guiding management and treatment in patients with RCC, as well as in predicting survival and progression. A more recent study confirmed the clinical role of FDG PET/CT in the restaging of RCC in a large group of patients (28). For recurrent and/or metastatic lesions in 104 patients, FDG PET/CT demonstrated sensitivity and specificity of 74 and 80%, respectively. FDG PET/CT findings affected management therapies in 45/104 cases (43%). In looking at overall survival (OS), positive FDG PET/CT associated with lower cumulative survival rates cover a 5-year period compared with that of negative FDG PET/CT. Likewise, a positive FDG PET/CT was associated with a lower 3-year progression-free survival (PFS) rate and was associated with high risk of progression, alone or in combination with disease stage or nuclear grading.

In patients with underlying primary malignancy, there is a high incidence of thrombosis, which can develop from venous thromboembolism (VTE) or more rarely, tumor thrombus. VTE is a common occurrence in cancer, managed with anticoagulant therapy, while tumor thrombosis requires aggressive multimodality therapeutics. Tumor thrombosis most commonly develops in solid tumors, such as RCC and hepatocellular carcinoma, adjacent to large veins as an extension of the malignancy and/or tumor infiltration (29). Sharma et al. conducted a retrospective review of FDG PET/CT scans in patients who had FDG-avid thrombosis (30). FDG PET/CT results were confirmed with clinical follow-up, structural imaging, and histopathology when available. On the basis of structural imaging and clinical follow-up, 10 patients had benign and 14 patients had tumor thrombosis. The most common site of thrombosis was the inferior vena cava. The mean SUV_{max} was 3.2 in the benign thrombosis group and 6.0 in the tumor thrombosis group. The difference in SUV_{max} was significant. In Ravina's series (31), out of 21 tumor thrombosis cases incidentally detected by FDG PET/CT, 6 were from RCCs. Ferda et al. also reported that FDG PET/CT successfully detected all 7 cases with tumor invasion into the inferior vena cava of 60 patients with RCC (19). The results showed that SUV and the pattern of FDG uptake are helpful for differentiating benign or bland emboli from tumor thrombosis in RCC patients, which is essential for management of patients (**Figure 1**).

Bone lesions associated with RCC are typically osteolytic. Traditional bone scintigraphy with Tc-99m methylene diphosphonate has limited sensitivity compared with FDG PET/CT, which has a higher sensitivity and a better accuracy in detecting bone metastases in patients with RCC. Wu et al. compared FDG PET with bone scan in 18 patients with biopsy-proven RCC and suspected bone metastases confirmed by histopathology or clinical follow-up of at least 1 year and conventional imaging or FDG PET/bone scans (32). Fifty-two bone lesions, 40 metastatic, and 12 benign, were found on either FDG-PET or bone scan. FDG PET accurately diagnosed all 40 metastatic and 12 benign bone lesions. In comparison, only 31 metastatic bone lesions were accurately detected by bone scan. FDG PET had 100% diagnostic sensitivity and 100% accuracy while that of bone scan were 77.5 and 59.6%, respectively.

18F-fluoro-2-deoxy-2-D-glucose (FDG) PET/CT can provide useful information and has a strong clinical role in the management of recurrent and metastatic RCC (**Figures 2–4**). In a 58-patient series reported by Rodriguez Martinez de Llano et al. (33), FDG PET/CT had the clinical impact in 25 cases (43%) and no impact in only 10 studies (17.2%). In more recently reported

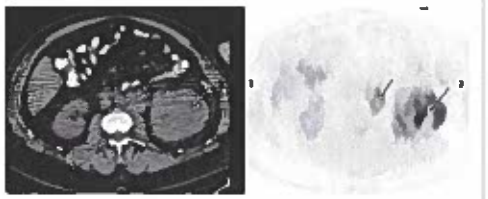

FIGURE 1 | Demonstration of primary RCC and tumor thrombosis on FDG PET/CT. A 53-year-old man had a large left renal mass seen on the CT. FDG PET/CT showed increased heterogeneous uptake of the mass in the left kidney. There was also tumor thrombosis in the renal vein, evidenced by FDG avid intraluminal lesion.

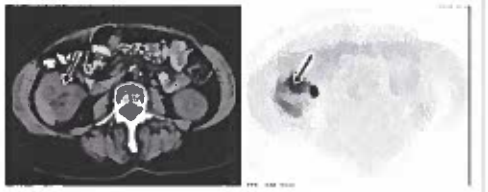

FIGURE 2 | Demonstration of RCC recurrence on FDG PET/CT. A 66-year-old woman had right partial nephrectomy for RCC. Two years later, a diagnostic CT showed a new mass in the anterior midpole of the right kidney, which was FDG avid on PET imaging. Subsequent nephrectomy confirmed recurrence of RCC.

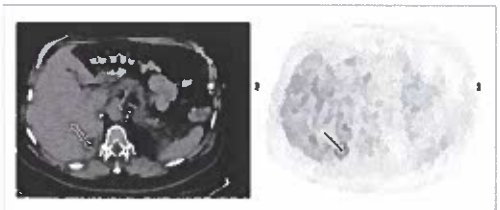

FIGURE 3 | Demonstration of RCC recurrence on FDG PET/CT. A 68-year-old man had right radical nephrectomy for RCC. FDG PET/CT was obtained for surveillance 5 years later, which showed a 2.0 cm density with moderate uptake in the surgical bed and was suspicious for recurrence. Surgical pathology revealed recurrent malignancy

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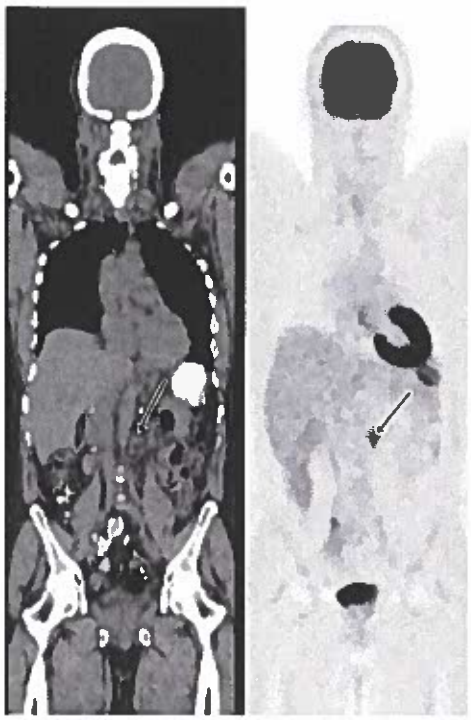

FIGURE 4 | Demonstration of metastatic lymph node on FDG PET/CT. A 57-year-old man had the left nephrectomy for RCC 5 years ago. A restaging FDG PET/CT showed a 1.5 cm left para-aortic node with moderate uptake. Subsequent node dissection confirmed metastasis.

large series by Alongi et al. (29), FDG PET/CT findings influenced therapeutic management in 45/104 cases (43%), treatment was switched from palliative to salvage in 12 patients, and new chemotherapy or immunotherapy was initiated in 24 patients.

Compared to conventional imaging modalities, FDG PET/CT has the advantage in detection of early metastatic disease and identification of musculoskeletal metastases, which are difficult to assess on CT and MRI. Bertagna et al. reported that histologically confirmed bone metastases were revealed at FDG PET/CT in the presence of negative diagnostic CT in 3 out of 27 cases (25). Park et al. compared FDG PET/CT to conventional imaging modalities for restaging 63 patients with RCC who have a high risk of local recurrence or distant metastasis (34). FDG PET/CT accurately classified the presence of a recurrence or metastasis in 56 (89%) patients. FDG PET/CT had 89.5% sensitivity, 83.3% specificity, 77.3% positive predictive value, 92.6% negative predictive value, and 85.7% accuracy in detecting recurrence or metastasis, which were similar to the results with conventional methods. Since FDG PET/CT is versatile and examines all organ systems with high accuracy in one procedure, and with no need for contrast agents, it might replace conventional methods for restaging RCC. Additionally, FDG PET/CT has a unique value in the prediction of survival and risk of progression in patients with recurrent or metastatic RCC (28).

However, FDG is not specific for malignant neoplasm. Increased uptake can be seen in many benign tumors and non-neoplastic processes. On FDG PET/CT for RCC, the false positive results are often due to concomitant inflammatory/infectious disease (9, 28), postoperative scar (26), postradiation inflammation, etc. The most common reason of a false negative FDG PET/CT finding is the small size of lesion and limited spatial resolution of PET scanner (26, 28). In RCC, another potential source of false negative result may be due to close proximity of the lesion to the urinary tract where there is physiologic urine activity (26).

FDG PET/CT FOR MONITORING THERAPEUTIC RESPONSE TO TYROSINE KINASE INHIBITOR

Adjuvant therapy remains a poor treatment alternative for advanced RCC. RCC is resistant to both conventional cytotoxic chemotherapy and radiation therapy, which carry a significant toxicity burden. However, a variety of targeted therapies including tyrosine kinase inhibitors (TKIs) have showed promising efficacy in advanced or metastatic RCC, with satisfactory results on PFS and quality of life (35, 36). TKIs, such as sunitinib and sorafenib, are antiangiogenic and can effectively inhibit tumor proliferation.

Although tumor size measurements with the response evaluation criteria in solid tumors (RECIST) criteria have been used for monitoring response to chemotherapy, there is often little change in size of the lesions, and some metastases even increase in size while the drug is prolonging survival (37). In the recent years, FDG PET/CT has been increasingly used to assess the therapeutic efficacy of TKIs in patients with metastatic RCC. According to Caldarella's systematic review of seven published studies, a good correlation was found between partial metabolic response and PFS and/or OS, with the highest survival rates in patients showing the greatest post-therapeutic reduction in SUV_{max} (38). In contrary, increase on FDG uptake was associated with lower OS (39). Pooled studies showed that FDG PET/CT had a high predictive value in the evaluation of response to SKI treatment in both skeletal and soft tissue lesions of metastatic RCC although there was heterogeneity of available data (38).

Some studies compared the values of FDG PET/CT and RECIST in predicting PFS and OS of patients treated with SKIs for metastatic RCC. Lyrdal et al. reported that FDG PET/CT was more useful than RECIST criteria, especially for the evaluation of skeletal lesions (40), as RECIST is limited to soft tissue lesions.

Kakizoe et al. reported that the decreased ratio of FDG accumulation of RCC lesions, as assessed 1 month following initiation of TKI treatment by FDG PET/CT, was not influenced by the site of RCC metastasis (41). The study suggests that TKIs can be used in the treatment of advanced RCC regardless of the metastatic site, and that FDG PET/CT is a useful method of surveillance to monitor therapeutic response in all lesions.

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CONCLUSION

Although the usefulness of FDG PET/CT in primary RCC remains unclear, and FDG PET/CT is not currently recommended for the diagnosis and staging of RCC based on updated national and international guidelines (42–44), it can effectively be used for postoperative surveillance and restaging as an adjunct when conventional imaging is not conclusive, as early diagnosis of recurrent/metastatic disease can drastically affect therapeutic decision and alter outcomes of patients (45). FDG uptake is helpful for differentiating benign or bland emboli from tumor thrombosis in RCC patients. FDG PET/CT has a higher sensitivity and accuracy in detecting bone metastases in patients with RCC than that of bone scan. Pretreatment SUV_{max} assessed by FDG PET/CT can provide helpful information for clinical decision-making as it can serve as a useful prognostic marker for patients with advanced RCC. High SUV_{max} in patients with primary RCC is suggested with correlate with a high likelihood of metastasis, and FDG accumulation may be useful in estimating patient's survival. In monitoring the efficacy of TKI treatment for advanced RCC, FDG PET/CT has been increasingly used to assess the therapeutic efficacy, and change of FDG uptake is a powerful index for evaluating the biological response to TKI.

AUTHOR CONTRIBUTIONS

The author confirms being the sole contributor of this work and approved it for publication.

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ATTACHMENT 12
Purpose of the Project

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Conflict of Interest Statement: The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

ATTACHMENT 13
Alternatives

Alternative #1: Maintain the Status Quo (do not purchase new major medical equipment)

This alternative has no capital costs associated with it but also yields no benefit to the community. This option would involve the waste of all of the resources and expenses that have been put into this project and would come at the expense of the improved quality of care this project is designed to generate – both in access to care but also in quality of information available regarding diagnosis and treatment. Hospitals and other centers would be unlikely to be capable of filling this avoidable gap in care, thus meaning that patients would go without necessary cancer treatments. UroPartners would like to avoid this option if at all possible.

Alternative #2: Wait to Replace Equipment until Failure and Modify the Project

Whether this alternative would have greater or lesser cost is unpredictable, ultimately, and unknown. It would likely result in increased costs because the additional expense associated with maintaining the current equipment would likely exceed any potential cost savings that could result from delay. More importantly, it would ensure patient disruption and result in a notable gap in available care because the applicants would have to proceed through the CON process upon the current equipment becoming obsolete. This would result in an unacceptably long period where necessary care and treatment would be unnecessarily unavailable. For these reasons, this alternative was not selected.

Alternative #3: Acquire only some of the Medical Equipment allowing for the Completion of the Project Below the CON Capital Expenditure Thresholds

Originally, when the project was first envisioned, Applicants completed the Board's Determination of Reviewability with counsel. The numbers were evaluated and this project, as envisioned, was able to be completed without HFSRB approval because the total cost involved fell below the Board's capital expenditure threshold. Being aware of and appreciating the obligations to comply with HFSRB process, when the final numbers came in, this conclusion was reevaluated. The total final cost exceeded the CON capital expenditure threshold, thus making this application for HFSRB approval warranted, absent redesigning the project. Were this Board not to approve the project, as proposed, the Applicants would have to consider only acquiring some of the proposed equipment – not for the purpose of bypassing the HFSRB process but – rather to ensure the most improvement of access to care that is envisioned by and described within this application. This alternative was not selected because the applicants believe the project, as proposed, has merit and warrants approval. Applicants are not unwilling to go through the CON process – to the contrary, it was their respect for and understanding of the CON process that allowed this project to begin without seeking HFSRB approval. It was that same appreciation that resulted in this Application because the expenses no longer fell below the capital expenditure threshold. However, Applicants clearly consider it preferrable to seek this approval than to re-design the project to avoid HFSRSB review. That is why this alternative was not selected.

Alternative #4: Project as Proposed

The project, as proposed, is the most responsible from a health planning perspective as well as from a patient care delivery perspective. This project enables the applicant to fulfil the CON principle of pursuing the most effective increase in access to care at the lowest appropriate cost. More importantly, it will ensure those patients reliant upon this exceptional practice group for their care will continue to have access to necessary life-improving and life-sustaining care. For those reasons, and given the deficiencies of the alternatives identified above, this is the alternative that was selected and is being presented to the Board for consideration and approval.

ATTACHMENT 14
Size of Project

SIZE OF PROJECT				
DEPARTMENT / SERVICE	**PROPOSED BGSF/DGSF**	**STATE STANDARD**	**DIFFERENCE**	**MET STANDARD?**
Diagnostic Radiology (Ultrasound, PET CT Machine,)	**464 GSF** Ultrasound Machine is mobile and not fixed equipment	**Total: 2,700 GSF** 1,800 GSF Per Unit (PET Scan); 900 GSF Per Unit (Ultrasound)	**2,236 GSF**	**YES**

The equipment that is the subject of this application will be installed at an existing physician office building operated by UroPartners. There is a total of 3,719 total GSF of clinical space identified in the facility which consists of physician office space where patients are provided with diagnosis and treatment. However, the space where the machines being installed will be located will only take a total of 464 GSF. The 464 GSF will be where the PET CT Scan will be located in the office, the ultrasound to be acquired is mobile and does not require fixed installation in the facility.

ATTACHMENT 15
Project Services Utilization

Pursuant to 77 Illinois Admin. Code Section 1110 Appendix B, the applicant is required to provide projected utilization to determine if the new equipment will meet Board target utilization standards for applicable clinical service areas.

As the PET CT Scan and Ultrasound will be utilized to provide imaging services that is the only applicable clinical service. To determine the project utilization of the new equipment the applicants reviewed their historical utilization for referrals to existing facilities that have said equipment.

On average during past calendar year, UroPartners sent 3,180 patients for scans utilizing both the PET CT Scan and Ultrasound machine. There is an expectation with the equipment now being located in-house, an increased need for these scans, and the new technological advances in medical condition diagnosis, there will be at least a 5% increase over historical volumes for the procedures utilizing the new equipment.

UTILIZATION					
	DEPARTMENT / SERVICE	**HISTORICAL UTILIZATION (PATIENT DAYS) (TREATMENTS) ETC.**	**PROJECTED UTILIZATION**	**STATE STANDARD**	**MEET STANDARD?**
YEAR 1	PET CT Scan Ultrasound	3,180 3,180	3,180 3,180	3,600 3,100	YES
YEAR 2	PET CT Scan Ultrasound	3,180 3,180	3,339 3,339	3,600 3,100	YES

ATTACHMENT 31
Necessary Expansion (c)(2)

The proposed project is necessary for the expansion of UroPartners acquisition and installation of a PET/CT scanner and a high-resolution ultrasound system at an existing UroPartners clinical facility. These two imaging modalities will be used in tandem to provide critical diagnostic and interventional support for patients with suspected or diagnosed urologic conditions, particularly prostate and kidney cancers.

To evaluate the need for this expansion, UroPartners reviewed its historical referral data to third-party facilities that currently offer PET/CT and ultrasound services. In the most recent full calendar year, UroPartners referred approximately 3,180 patients for diagnostic imaging procedures involving either PET/CT, ultrasound, or both. Based on internal projections, clinical demand, and increased efficiency from onsite availability, the practice conservatively estimates a minimum 5% increase in utilization once the equipment is installed in-house—bringing expected annual volumes to over 3,300 scans. This increase reflects anticipated improvements in care coordination, access, and clinical outcomes.

UroPartners is expanding the scope of services it offers by incorporating Prostate-Specific Membrane Antigen (PSMA) PET imaging, kidney scans for clear cell renal cell carcinoma (ccRCC), and interventional radiology procedures such as fibroid embolization and stent removal. These services represent current standards of care in modern urologic oncology and are increasingly recommended by national organizations such as the American Urological Association (AUA) and the National Comprehensive Cancer Network (NCCN). The PSMA PET scan, for instance, has rapidly become the gold standard in prostate cancer imaging, offering superior sensitivity and specificity compared to conventional imaging for both initial staging and recurrence detection.

Moreover, the FDA is expected to approve a new ccRCC-specific imaging agent in August 2025, which will further expand the diagnostic capabilities of the PET/CT scanner and allow UroPartners to offer state-of-the-art non-invasive imaging for kidney cancer—replacing the need for more invasive procedures and unnecessary hospital referrals.

The equipment will be installed in compliance with all applicable building codes, life safety standards, and licensure regulations. The PET/CT scanner will be located within 464 GSF of existing clinical space at the UroPartners facility. No fire code deficiencies or licensure violations are currently cited for the proposed installation site, and the practice is working with licensed architects and qualified health physicists to ensure proper shielding, radiation safety compliance, and structural integration. Installation plans and vendor documentation will be submitted to IDPH as part of the licensing and inspection process.

ATTACHMENT 31
Utilization – Major Medical Equipment (c)(3)(A)

The Applicants meet the requirements of 77 Ill. Adm. Code § 1110.270(c)(3)(A), as the proposed acquisition of major medical equipment—a PET/CT scanner and a high-resolution ultrasound system—is both necessary for the geographic service area and projected to achieve applicable target utilization levels within 12 months of installation. These projections are supported by a robust and well-documented referral base, a high-volume patient population, and an increasing demand for advanced imaging procedures associated with the diagnosis and treatment of urologic conditions.

UroPartners referred approximately 3,180 patients in the most recent calendar year for procedures utilizing PET/CT and ultrasound imaging. With the acquisition and in-house operation of this equipment, the Applicants project at least a 5% increase in utilization, resulting in more than 3,300 procedures annually across the PET/CT and ultrasound modalities. This projection is based on improved access, faster turnaround times, and enhanced patient management—all of which will encourage internal referrals and greater procedural efficiency. The Applicants are confident that this volume will support full utilization of the equipment as defined in the applicable IDPH standards for imaging modalities.

While Appendix B of the Board's rules does not include specific utilization benchmarks for office-based PET/CT or ultrasound services provided in a non-hospital setting, the Applicants have provided detailed projected utilization based on historical referral patterns and regional incidence rates of prostate and kidney cancer—two conditions that represent the majority of imaging needs addressed by this equipment. According to the Illinois Department of Public Health, prostate cancer is the most common cancer in men in the state, with approximately 10,000 new cases annually. Kidney cancer, particularly clear cell renal cell carcinoma (ccRCC), represents another significant source of diagnostic need, with more than 2,000 new cases reported annually in Illinois.

In addition, the expansion of imaging capabilities will support a growing interventional radiology program and allow UroPartners to offer advanced procedures such as PSMA PET scans, fibroid embolizations, stent removals, and kidney cancer diagnostics—each of which requires high-quality diagnostic imaging to be performed safely and effectively. The combination of historical referral volume, regional disease incidence, and increased diagnostic and interventional capability supports the projected utilization of this equipment well within the required 12-month timeframe.

ATTACHMENT 33
Availability of Funds

The applicants have sufficient resources to fund the cash portion of this project. Attached as evidence is a letter from JP Morgan, the Applicant's financial institution which reflects that the Applicant has sufficient funds on hand to complete the project.

ATTACHMENT 33
Availability of Funds

J.P.Morgan

Solaris Health Holdings LLC
2101 West Commercial Boulevard, Suite 3500
Fort Lauderdale, FL 33309

Dear Sir or Madam,

This letter is being delivered to you to provide information on the Company's banking relationship with JPMorgan Chase Bank, N.A (the "Bank").

We can hereby confirm that the Company has maintained accounts at the Bank since 2020 and has operated the accounts in a satisfactory manner.

As of 5/30/20255, the Company maintains balance in the mid to high 8 figures.

Please be advised that this letter refers only to facts as they exist as of the date of this letter and the Bank shall have no duty or obligation to inform the addressee hereof of any future changes in such facts. This letter is solely for the benefit of the addressee hereof for the referenced purpose, and may not be relied on by any other person or for any other purpose.

Sincerely,

Vince Secret
Executive Director
JPMorgan Chase Bank, N.A.
450 S. Orange Ave, Floor 10
Orlando, FL 32801
407.236.7090
vincent.secret@jpmorgan.com

ATTACHMENT 35
Financial Viability

The applicants meet the requirements for a financial viability waiver in accordance with 77 Ill. Adm. Code § 1120.130, as the proposed project will be funded by internal sources of the Applicant.

ATTACHMENT 36
Economic Feasibility

June 2, 2025

John P. Kniery
Board Administrator
Illinois Health Facilities and Services Review Board
525 W Jefferson Street, Floor 2
Springfield, IL 62761

Re: UroPartners Imaging Center
Ill. Admin. Code Section 1120.120(a) Available Funds Certification
Ill. Admin. Code Section 1120.140(a) Reasonableness of Financing Arrangements

Dear Mr. Kniery:

As a representative of UroPartners Imaging Center, I, Jason Langley, hereby attest that the project costs will be $5,753,206. Applicants will fund the entire project and the necessary working capital and operating deficits with existing cash and securities. All applicants have sufficient and readily accessible internal resources to fund the obligation required by the project.

I further certify that our analysis of the funding options for this project reflected that the funding strategy outlined herein is the lowest net cost option available.

Sincerely,

Jason Langley
Chief Financial Officer
Solaris Health Holdings, LLC

ATTACHMENT 36
Economic Feasibility

COST AND GROSS SQUARE FEET BY DEPARTMENT OR SERVICE									
Department (List below)	A	B	C	D	E	F	G	H	Total Cost (G + H)
	Cost/Square Foot New	Cost/Square Foot Mod.	Gross Sq. Ft. New	Gross Sq. Ft. Circ.*	Gross Sq. Ft. Mod.	Gross Sq. Ft. Circ.*	Const. $ (A x C)	Mod. $ (B x E)	
Diagnostic Equipment (Ultrasound and PET CT Scan)		$461.41			3,719			$1,715,991	$1,715,991
Contingency		$45.71			3,719			$170,000	$170,000
TOTALS		$507.12			3,719			$1,885,991	$1,885,991
* Include the percentage (%) of space for circulation									

ATTACHMENT 37
Safety Net Impact Study

Pursuant to 77 Ill. Admin Code Section 1110.20 the acquisition of major medical equipment is classified as a non-substantive project. As a non-substantive project for the acquisition of major medical equipment, the submission of a safety net impact study is not required by the applicants pursuant to 77 Illinois Admin. Code Section 1110.10(c).

ATTACHMENT 38
Charity Care

The applicant, UroPartners, LLC is a physician practice group and UroPartners Imaging Center is an office-based lab clinical setting. The facility is not considered a health care facility as defined by the board and thus does not collect charity care data. However, the Applicants do operate the UroPartners Surgery Center and the charity care information for that facility is listed below.

CHARITY CARE			
	2020	2021	2022
Net Patient Revenue	**$8,713,525**	**$9,956,553**	**$10,415,839**
Amount of Charity Care (charges)*	$0	$0	$0
Cost of Charity Care	$0	$0	$0

* To be clear, it is not that UroPartners does not engage in Charitable care or other organized efforts to provide charitable contributions, both institutionally and through its individual physicians. However, the care provided, and process utilized does not meet the Board's definition of Charity Care and, as such, cannot be reported as Charity Care.

ATTACHMENT 39
Flood Plain Requirements

June 2, 2025

John P. Kniery
Board Administrator
Illinois Health Facilities and Services Review Board
525 W Jefferson Street, Floor 2
Springfield, IL 62761

Re: UroPartners Pathology Lab - Flood Plain Requirements

Dear Mr. Kniery:

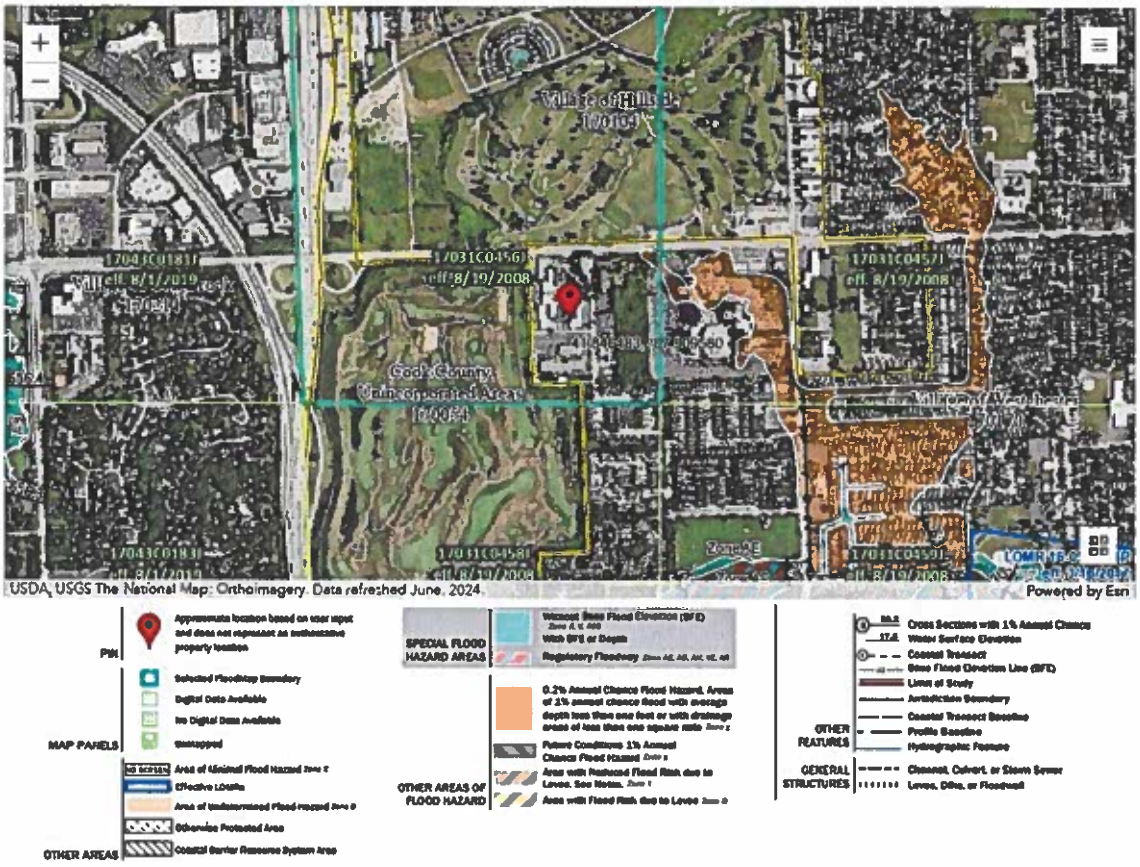
As representative of UroPartners, LLC, I, Daniel Scharff, affirm that our facility complies with Illinois Executive Order #2005-5. The facility located at 2225 Enterprise Drive, Suite 2511 Westchester, Illinois 60154 is not located in a flood plain, as evidence please find enclosed a map from the Federal Emergency Management Agency ("FEMA").

I hereby certify this true and is based upon my personal knowledge under penalty of perjury and in accordance with 735 ILCS 5/1-109.

Sincerely,

Daniel Scharff
Secretary
UroPartners, LLC

ATTACHMENT 39
Flood Plain Requirements



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