26-032

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HEALTH FACILITIES &

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: Advanced Radiation Center of Chicago		
Street Address: 8915 W. Golf Road		
City and Zip Code: Niles, 60714		
County: Cook	Health Service Area: 007	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: Illinois Corporation Service Company
Registered Agent Street Address: 801 Adlai Stevenson Drive
Registered Agent City and Zip Code: Springfield, 62703
Name of President: Justin Cohen, M.D.
President Street Address: 2245 Enterprise Drive, Suite 4506
President City and Zip Code: Westchester, 60154
President Telephone Number: (708) 492-0502

Type of Ownership of Applicants

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

LLINOIS 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: Advanced Radiation Center of Chicago		
Street Address: 8915 W. Golf Road		
City and Zip Code: Niles, 60714		
County: Cook	Health Service Area: 007	Health Planning Area: 031

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

Exact Legal Name: Solaris Health Holdings, LLC
Street Address: 2101 W. Commercial Boulevard, Suite 3500
City and Zip Code: Fort Lauderdale, 33309
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 CEO: James Weber, M.D.
CEO Street Address: 500 E. Broward Boulevard, Suite 2150
CEO City and Zip Code: Fort Lauderdale, 33394
CEO Telephone Number: (708) 492-0502

Type of Ownership of Applicants

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

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E-mail Address: JMorado@beneschlaw.com and MSilberman@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) 495-0585

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) 495-0585

Site Ownership [Provide this information for each applicable site]

Exact Legal Name of Site Owner: MOB Niles A Delaware
Address of Site Owner: 2901 Butterfield Road, Oak Brook, IL 60523
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: Advanced Radiation Center of Chicago
Address: 8915 W. Golf Road, Niles, IL 60523

☐	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 Acquisition of Major Medical Equipment by UroPartners, LLC who will be operating Advanced Radiation Center of Chicago ("ARCC") to be located at 8915 W. Golf Road in Niles, Illinois 60714. Specifically, the project by UroPartners, LLC includes the acquisition of major medical equipment pursuant to 77 Ill. Admin. Code 1110.270(a)(2)(c)(3)(A). Solaris Health Holdings, LLC will be guaranteeing the funding for the acquisition.

This major medical equipment includes a Varian Ethos Machine (LINAC) and a SOMATON.go CT SIM from Siemens, and other ancillary capital 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	$850,000	$400,000	$1,250,000
Modernization Contracts	-	-	-
Contingencies	$80,000	$40,000	$120,000
Architectural/Engineering Fees	$47,312	$127,688	$175,000
Consulting and Other Fees	-	-	-
Movable or Other Equipment (not in construction contracts)	$5,410,000	$750,000	$6,160,000
Bond Issuance Expense (project related)	-	-	-
Net Interest Expense During Construction (project related)	-	-	-
Fair Market Value of Leased Space or Equipment	$250,000	$674,000	$924,000
Other Costs to Be Capitalized	-	-	-
Acquisition of Building or Other Property (excluding land)	-	-	-
TOTAL USES OF FUNDS	$6,637,312	$1,991,688	$8,629,000
SOURCE OF FUNDS	**CLINICAL**	**NONCLINICAL**	**TOTAL**
Cash and Securities	$6,387,312	$1,317,688	$7,705,000
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)	$250,000	$674,000	$924,000
Governmental Appropriations	0	0	0
Grants	0	0	0
Other Funds and Sources	0	0	0
TOTAL SOURCES OF FUNDS	**$6,387,312**	**$1,991,688**	**$8,629,000**
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: NOT APPLICABLE

Fair Market Value: NOT APPLICABLE

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 NOT APPLICABLE

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, 2027

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	6,637,312	-	1,574	1,574	-	-	-
Total Clinical	6,637,312	-	1,574	1,574	-	-	-
NON-REVIEWABLE							
Administrative	1,991,688	-	4,248	4,248	-	-	-
Total Non-clinical	1,991,688	-	4,248	4,248	-	-	-
TOTAL	**8,629,000**	**-**	**5,822**	**5,822**	**-**	**-**	**-**

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: Advanced Radiation Center of Chicago			**CITY:** Niles		
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

Justin Cohen, M.D.
PRINTED NAME

President
PRINTED TITLE

Notarization:
Subscribed and sworn to before me
this 30th day of May 2026

Signature of Notary

Seal

OFFICIAL SEAL
BRADLEY A KATZ
Notary Public - Illinois
Commission No. 754097
My Commission Expires August 15, 2027

SIGNATURE

Richard Harris, M.D.
PRINTED NAME

Member
PRINTED TITLE

Notarization:
Subscribed and sworn to before me
this _____ day of _____

Signature of Notary

Seal

*Insert the EXACT legal name of the applicant

CERTIFICATION

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

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- in the case of estates and trusts, two of its beneficiaries (or the sole beneficiary when two or more beneficiaries do not exist); and
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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	SIGNATURE
Justin Cohen, M.D.	Richard Harris, M.D.
PRINTED NAME	PRINTED NAME
President	Member
PRINTED TITLE	PRINTED TITLE
Notarization: Subscribed and sworn to before me this _____ day of _____	Notarization: Subscribed and sworn to before me this 4th day of June, 2026
Signature of Notary	Signature of Notary
Seal	Seal

CARMEN M CORONADO
Official Seal
Notary Public - State of Illinois
My Commission Expires Sep 12, 2026

*Insert the EXACT legal name of the applicant

CERTIFICATION

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- 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	SIGNATURE
James Weber, M.D. PRINTED NAME	Josh Peck PRINTED NAME
Chief Executive Officer PRINTED TITLE	Chief Operating Officer PRINTED TITLE
Notarization: Subscribed and sworn to before me this 27th day of May	Notarization: Subscribed and sworn to before me this _____ day of _____
Signature of Notary	Signature of Notary
Seal Jennifer Sutton My Commission Expires 1/23/2027 Notary ID 123585?2	Seal

*Insert 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.

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SIGNATURE	SIGNATURE
James Weber, M.D. PRINTED NAME	Josh Peck PRINTED NAME
Chief Executive Officer PRINTED TITLE	Chief Operating Officer PRINTED TITLE
Notarization: Subscribed and sworn to before me this _____ day of _____	Notarization: Subscribed and sworn to before me this 15th day of June, 2026
Signature of Notary	Signature of Notary
Seal	Seal

CARMEN M CORONADO
Official Seal
Notary Public - State of Illinois
My Commission Expires Sep 12, 2026

*Insert the EXACT 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 (LINAC and CT Machine,)	**1,574**	**Total: 4,200** 2,400 GSF Per Unit (Accelerator); 1,800 GSF Per Unit (CT Scan)	**-2,626**	**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	Accelerator CT Scan	3,000 procedures (Accelerator) 3,000 procedures (CT Scan)	3,000 procedures (Accelerator) 3,000 procedures (CT Scan)	7,500 procedures (Accelerator) 7,000 (CT Scan)	YES
YEAR 2	Accelerator CT Scan	3,000 procedures (Accelerator) 3,000 procedures (CT Scan)	3,000 procedures (Accelerator) 3,000 procedures (CT Scan)	7,500 procedures (Accelerator) 7,000 procedures (CT Scan)	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
☒ **CT Scan/ Accelerator**	-	**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
APPEND 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]:**

$7,705,000	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.
$924,000	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.
$8,629,000	**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 NUMERIC SEQUENTIAL 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		Gross Sq. Ft.		Gross Sq. Ft.		Const. $ (A x C)	Mod. $ (B x E)	
	New	Mod.	New	Circ.*	Mod.	Circ.*			
Diagnostic Equipment (LINAC and CT Scan)	$540.03	-	1,574	-	-	-	$850,000	-	$850,000
Contingency	$50.83	-	1,574	-	-	-	$80,000	-	$80,000
TOTALS	$590.85	-	1,574	-	-	-	$930,000	-	$930,000

* 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 – NOT APPLICABLE

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 NOT APPLICABLE			
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 – NOT APPLICABLE

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: Advanced Radiation Center of Chicago (Name) 8915 W. Golf Road (Address)

   Niles (City) IL (State) 60714 (ZIP Code) (708) 492-0565 (Telephone Number)

2. Project Location: 8915 W. Golf Road (Address) Niles (City) IL (State)

   Cook (County) Niles (Township) (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:

INDEX OF ATTACHMENTS

ATTACHMENT 1
Certificate of Good Standing

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

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

ATTACHMENT 1
Certificate of Good Standing - UroPartners, LLC

File Number 0142447-5

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* 17TH *day of* MAY *A.D.* 2026 .

Authentication #: 261370041B verifiable until 05/17/2027
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.

SEAL OF THE STATE OF ILLINOIS
AUG. 26TH 1818

In Testimony Whereof, *I hereto set my hand and cause to be affixed the Great Seal of the State of Illinois, this* 17TH *day of* MAY *A.D.* 2026 .

Authentication #: 2613700428 verifiable until 05/17/2027
Authenticate at: https://www.ilsos.gov

SECRETARY OF STATE

ATTACHMENT 2
Site Ownership

The Applicant will be subleasing space from Physician Reliance, LLC, which holds an active lease with property owners. MOB Niles A Delaware, LLC is the current property owner. Attached as evidence of ownership is a copy of the existing tax bill for the site.

TOTAL PAYMENT DUE

$0.00
By 06/01/26

2025 First Installment Property Tax Bill - Cook County Electronic Bill

Property Index Number (PIN)	Volume	Code	Tax Year	(Payable In)	Township	Classification
09-15-201-019-0000	088	22044	2025	(2026)	Maine	5-92

IF PAYING LATE, PLEASE PAY	06/02/26-07/01/26	07/02/26-08/01/26	08/02/26-09/01/26	LATE INTEREST IS 0.75% PER MONTH, BY STATE LAW
	$0.00	$0.00	$0.00	

TAXING DISTRICT DEBT AND FINANCIAL DATA

Your Taxing Districts	Money Owed by Your Taxing Districts	Pension and Healthcare Amounts Promised by Your Taxing Districts	Amount of Pension and Healthcare Shortage	% of Pension and Healthcare Costs Taxing Districts Can Pay
NORTHWEST MOSQUITO ABATEMENT DISTRICT	$362,063	$9,328,682	$696,896	92.53%
METRO WATER RECLAMATION DIST OF GR CHGO	$3,248,879,000	$3,303,258,000	$1,444,138,000	56.28%
NORTH MAINE FIRE PROTECTION DISTRICT	$1,448,842	$46,328,192	$14,270,851	69.20%
NILES-MAINE DISTRICT LIBRARY	$558,097	$6,399,698	$112,509	98.24%
GOLF MAINE PARK DISTRICT	$182,025	$2,987,890	$256,328	91.42%
MAINE TOWNSHIP HIGH SCHOOL 207	$185,861,180	$135,642,413	$3,500,207	97.42%
SCHOOL DISTRICT 63	$61,211,582	$39,017,659	$1,746,471	95.52%
TOWN MAINE	$1,482,493	$13,253,441	$0	102.02%
FOREST PRESERVE DISTRICT OF COOK COUNTY	$214,441,242	$617,834,550	$382,643,760	38.07%
COUNTY OF COOK	$14,499,553,496	$21,406,518,462	$8,452,341,655	60.52%
TOTALS:	$18,331,212,471	$25,596,039,750	$10,299,438,412	

For a more in-depth look at government finances and how they affect your taxes, visit *cookcountytreasurer.com*

PAY YOUR TAXES ONLINE
Pay at cookcountytreasurer.com from your bank account or credit card.

IMPORTANT MESSAGES

TAX CALCULATOR

2024 TOTAL TAX		258,611.89
2025 ESTIMATE	X	55%
2025 1st INSTALLMENT	=	141,246.53

The First Installment amount is 55% of last year's total taxes. All exemptions, such as homeowner and senior exemptions, will be reflected on your Second Installment tax bill.

PROPERTY LOCATION

8915 GOLF RD
NILES IL 60714

MAILING ADDRESS

MOB NILES A DELAWARE
2901 BUTTERFIELD RD
OAK BROOK IL 60523-1106

*** Please see 2025 First Installment Payment Coupon next page ***

ATTACHMENT 3
Facility Ownership

The facility shall operate as Advanced Radiation Center of Chicago, which is owned and operated by UroPartners, LLC. Included with this Attachment is the facility owner's Certificate of Good Standing.

File Number 0142447-5

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*

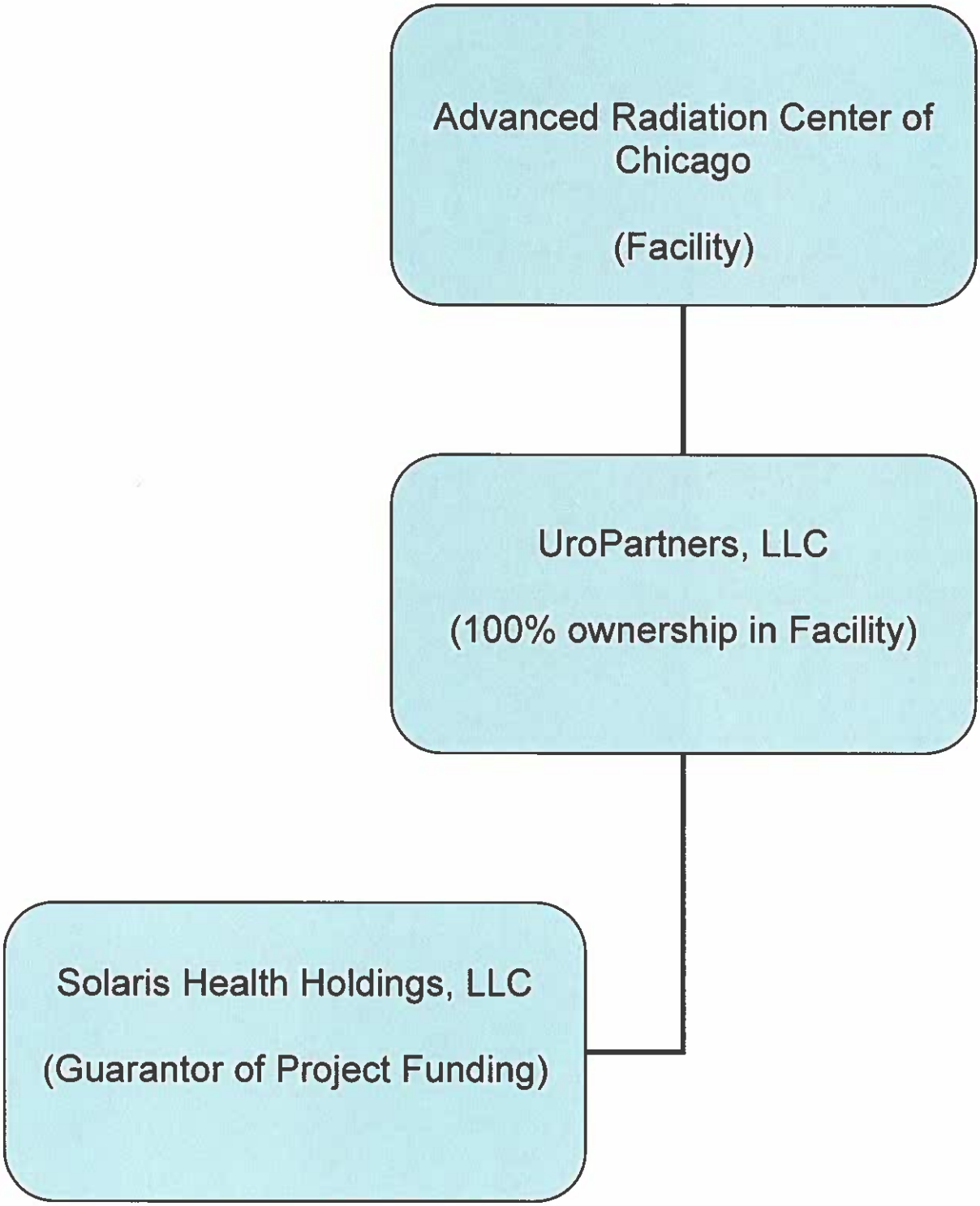
UROPARTNERS, LLC. HAVING ORGANIZED IN THE STATE OF ILLINOIS ON FEBRUARY 10, 2005, APPEARS TO HAVE COMPLIED WITH ALL PROVISIONS OF THE LIMITED LIABILITY COMPANY ACT OF THIS STATE, AND AS OF THIS DATE IS IN GOOD STANDING AS A DOMESTIC LIMITED LIABILITY COMPANY IN THE STATE OF ILLINOIS.

In Testimony Whereof, *I hereto set my hand and cause to be affixed the Great Seal of the State of Illinois, this* 17TH *day of* MAY *A.D.* 2026 .

Authentication #: 2613700418 verifiable until 05/17/2027
Authenticate at: https://www.ilsos.gov

SECRETARY OF STATE

ATTACHMENT 4
Site Ownership



May 21, 2026

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

Re: Advanced Radiation Center of Chicago - Flood Plain Requirements

Dear Mr. Kniery:

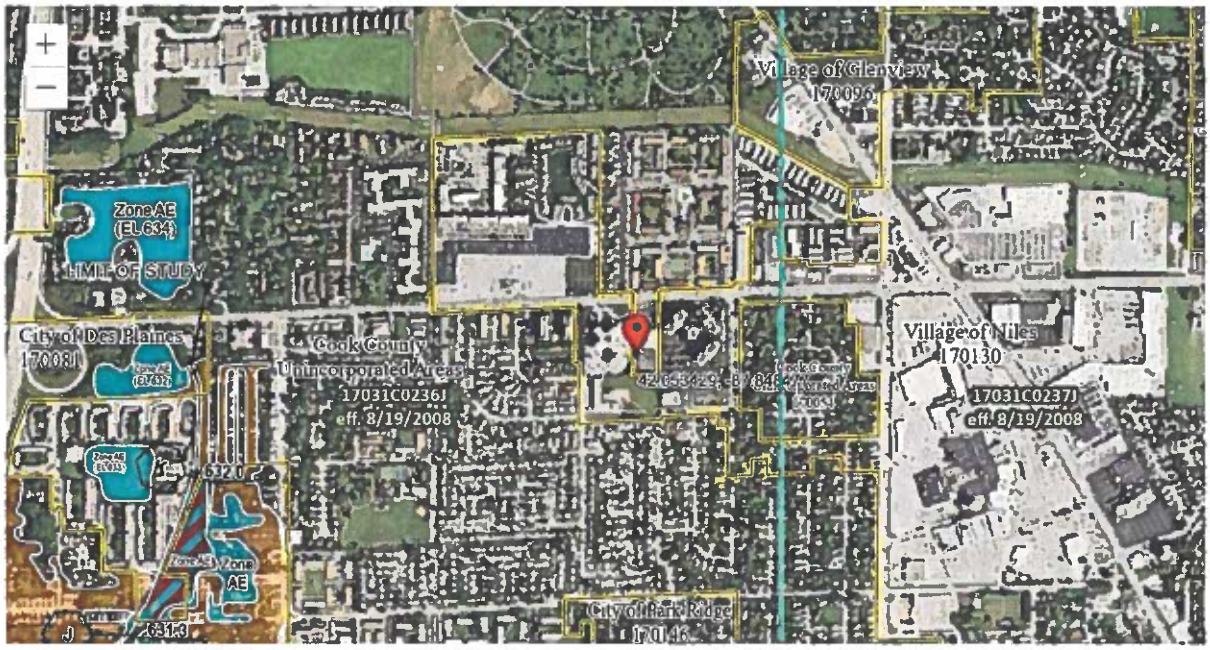
As representative of Advanced Radiation Center of Chicago, I, Justin Cohen, M.D., affirm that our proposed site complies with Illinois Executive Order #2005-5. The site located at 8915 West Golf Road, Niles, Illinois 60714 is not located in a flood plain, as evidence please find enclosed a map from the Federal Emergency Management Agency ("FEMA").

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

Sincerely,

Justin Cohen, M.D.
President
UroPartners, LLC

ATTACHMENT 5
Flood Plain Requirements



ATTACHMENT 6
Historical Preservation Letter

The applicant submitted a request for determination to the Illinois Department of Natural Resources-Preservation Services Division on May 15, 2026. A final determination has been received as of the filing of this application and is included in this attachment.

Cook County
Niles
CON - Advanced Radiation Center of Chicago Medical Equipment
8915 W. Gold Rd.

IHFSRB, SHPO Log #001051926

May 20, 2026

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 or archaeological sites exist within the project area.

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, IL 60606
Direct Dial: 312.212.4967
Fax: 312.757.9192
jmorado@beneschlaw.com

May 15, 2026

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 Major Medical Equipment

Dear Mr. Kruchten:

I am writing on behalf of my client, Advanced Radiation Center of Chicago 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.). Advanced Radiation Center of Chicago is submitting an application for a Certificate of Need from the Illinois Health Facilities and Services Review Board. Advanced Radiation Center of Chicago seeks to purchase major medical equipment for a radiation laboratory to be located in an existing medical office building located at 8915 West Golf Road, Niles, IL 60714.

The radiation laboratory is purchasing major medical equipment which requires a CON application and will be building out within the existing space. 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.

If you have any questions or need any additional information regarding the project, please feel free to contact me via phone at 312-212-4967 or via email at JMorado@beneschlaw.com

ATTACHMENT 6
Historical Preservation Letter

Very truly yours,

BENESCH, FRIEDLANDER,
COPLAN & ARONOFF LLP

Juan Morado Jr.

ATTACHMENT 6
Historic Preservation Act Requirements

May 15, 2026
Page 3

Topographical Map
8915 West Golf Road, Niles, IL 60714

ATTACHMENT 6
Historic Preservation Act Requirements

Aerial Map
8915 West Golf Road, Niles, IL 6071

ATTACHMENT 6
Historical Preservation Act Requirements

May 15, 2026
Page 5

Street view of property
8915 West Golf Rd, Niles, IL 60714

28634879 v1

ATTACHMENT 6
Historical Preservation Act Requirements

May 15, 2026
Page 6

3D Aerial view
8915 West Golf Road, Niles, IL 60714

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	$850,000	$400,000	$1,250,000
Modernization Contracts	-	-	-
Contingencies	$80,000	$40,000	$120,000
Architectural/Engineering Fees	$47,312	$127,688	$175,000
Consulting and Other Fees	-	-	-
Movable or Other Equipment (not in construction contracts)	$5,410,000	$750,000	$6,160,000
Bond Issuance Expense (project related)	-	-	-
Net Interest Expense During Construction (project related)	-	-	-
Fair Market Value of Leased Space or Equipment	$250,000	$674,000	$924,000
Other Costs to Be Capitalized	-	-	-
Acquisition of Building or Other Property (excluding land)	-	-	-
TOTAL USES OF FUNDS	$6,637,312	$1,991,688	$8,629,000
SOURCE OF FUNDS	**CLINICAL**	**NONCLINICAL**	**TOTAL**
Cash and Securities	$6,387,312	$1,317,688	$7,705,000
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)	$250,000	$674,000	$924,000
Governmental Appropriations	0	0	0
Grants	0	0	0
Other Funds and Sources	0	0	0
TOTAL SOURCES OF FUNDS	**$6,387,312**	**$1,991,688**	**$8,629,000**
NOTE: ITEMIZATION OF EACH LINE ITEM MUST BE PROVIDED AT ATTACHMENT 7, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.			

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 increases in labor and raw material costs nationwide, 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 $850,00 or $540.03 per clinical square foot.

Contingencies - The Project's contingencies costs are designed to allow the construction team an amount of funding for unforeseeable events related to construction. Clinical construction costs for contingencies are estimated to be $80,000 or 9.4% of projected clinical new construction costs.

Architectural/Engineering Fees - The clinical project cost for architectural/engineering fees are projected to be $147,312 or 5.1% 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.

CT Machine	$610,000
Linear Accelerator	$4,800,000

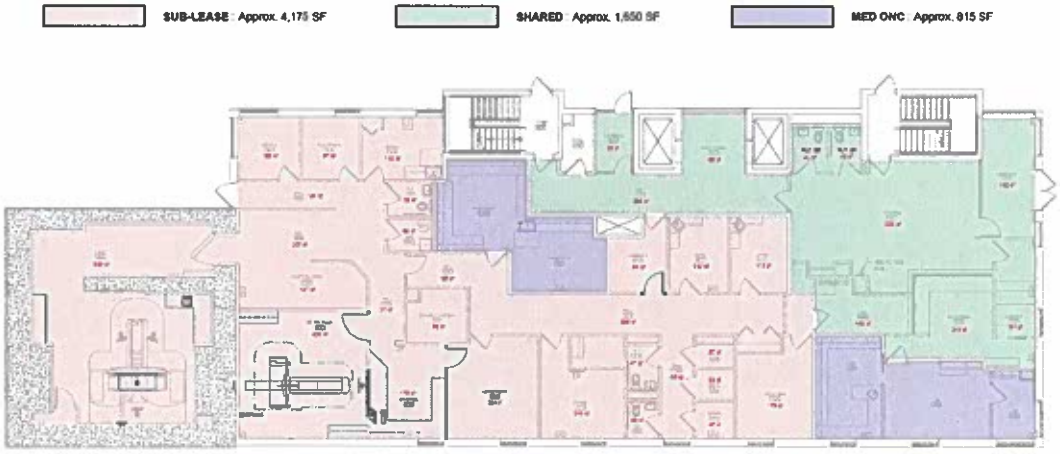
Fair Market Value of Leased Space - The Project includes leased space necessary for the operation of the proposed service. The fair market value of the leased space is based on the fixed rental payments required under the lease term through November 2030. The lease provides for annual fixed rent of $184,804.40, which is equal to a monthly fixed rent of $15,400.36, for each of the first five lease years.

Accordingly, the fair market value of the leased space remains constant throughout Years 1 through 5 of the lease term. These lease costs have been identified and included as part of the Project's overall cost in accordance with applicable CON requirements regarding the valuation of leased property.

Lease Year	Annual Fixed Rent	Monthly Fixed Rent
Year 1	$184,804.40	$15,400.36
Year 2	$184,804.40	$15,400.36
Year 3	$184,804.40	$15,400.36
Year 4	$184,804.40	$15,400.36
Year 5	$184,804.40	$15,400.36

ATTACHMENT 8
Project Status and Completion Status

The proposed project plans are still at a schematic stage. The proposed completion date is July 1, 2027. Financial commitment for the project will occur following permit issuance, but in accordance with HFSRB regulations.



ATTACHMENT 9
Cost Space Requirements

The equipment to be installed within the existing building will account for approximately 1,574 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	6,637,312	-	1,574	1,574	-	-	-
Total Clinical	6,637,312	-	1,574	1,574	-	-	-
NON-REVIEWABLE							
Administrative	1,991,688	-	4,248	4,248	-	-	-
Total Non-clinical	1,991,688	-	4,248	4,248	-	-	-
TOTAL	**8,629,000**	**-**	**5,822**	**5,822**	**-**	**-**	**-**

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.

Advanced Radiation Center of Chicago

Advanced Radiation Center of Chicago ("ARCC" or the "Facility") is a dedicated radiation treatment facility operated by UroPartners, LLC, one of the largest independent urology group practices in the Midwest. The Facility was established to meet the highly specialized treatment needs of patients requiring radiation therapy, building upon UroPartners' extensive experience in radiation oncology through its Prostate Centers of Excellence and its broad provider network.

The Facility will provide radiation therapy services for patients diagnosed with breast, lung, gastrointestinal, gynecological, and urologic cancers. By centralizing radiation services under one specialized center, UroPartners and its affiliated physicians ensure treatment consistency, clinical accuracy, and coordinated care—key factors in the effective management of these malignancies and other complex conditions. The Facility's integration into the broader UroPartners system enables seamless communication between radiation oncologists and referring physicians, enhancing real-time decision-making and improving overall patient outcomes.

UroPartners intends to acquire major medical equipment for the Facility located at 8915 West Golf Road, Niles, IL 60714.

UroPartners, LLC

UroPartners, LLC is the leading independent urology group in the Midwest, comprising of 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 of Excellence, surgical affiliations, and an in-house pathology laboratory that collectively serve 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 Pathology Laboratory, 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 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 and provide the clinical foundation upon which the proposed Facility is built.

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.

The Specialty Alliance

UroPartners is a member of The Specialty Alliance, a physician-led organization that supports independent specialty practices by providing the infrastructure, resources, and strategic scale needed to grow while preserving physician leadership and clinical independence. Built for specialists by specialists, The Specialty Alliance empowers leading physician-led groups in gastroenterology, urology, and other specialties to thrive through thoughtful expansion, shared capabilities, and innovation without compromising clinical autonomy.

ATTACHMENT 11
Background of the Applicant

The Specialty Alliance is designed to enable physicians to focus on what matters most: delivering exceptional patient care. Through operational expertise, strategic capital, and centralized infrastructure, the organization reduces administrative burden and positions its member practices for sustainable growth and continued clinical advancement. Its support model encompasses practice management, revenue cycle optimization, information technology, compliance, human resources, and strategic planning services allowing physician groups like UroPartners to direct their energy toward clinical excellence and expansion of services.

For purposes of this application, UroPartners' affiliation with The Specialty Alliance demonstrates access to the financial resources, operational capacity, and organizational infrastructure necessary to support the acquisition of major medical equipment and the successful operation of the proposed Facility. The Specialty Alliance's proven track record of supporting independent specialty practices through growth initiatives provides additional assurance that ARCC will be managed with the administrative discipline and financial sustainability required to serve the community over the long term.

Parthiv Mehta, M.D.

Parthiv Mehta, M.D. will serve as lead physician at the proposed Facility. Dr. Mehta is a Board-Certified Radiation Oncologist specializing in the treatment of prostate cancer, with expertise and advanced training in intensity-modulated radiation therapy (IMRT), image-guided radiation therapy (IGRT), and prostate brachytherapy. He is also an expert in utilizing The Calypso® 4D Localization System (GPS for the body).

Dr. Mehta earned his bachelor's degree in engineering from the University of Michigan before entering the Medical Scholars Program at the University of Illinois, where he completed both an M.D. and an M.B.A. He completed his residency in radiation oncology at Rush University Medical Center and a brachytherapy fellowship at Beth Israel Medical Center in New York City. During his training, he completed research that has been published in several peer-reviewed clinical journals.

Dr. Mehta is a member of the American Society for Therapeutic Radiology and Oncology, the American Society of Clinical Oncology, the American Medical Association, the Radiological Society of North America, the American College of Radiation Oncology, and the American Brachytherapy Society. He has earned numerous accolades, including Castle Connolly Regional Top Doctors, Chicago Magazine's Top Cancer Doctors in Chicago, and Chicago Magazine's Top Doctors in Chicago.

Dr. Mehta is committed to providing his patients with the highest quality, cutting-edge treatment options while ensuring they are thoroughly informed about their treatment choices. His extensive experience in radiation oncology and his leadership within UroPartners' existing Prostate Centers of Excellence position him to effectively oversee the clinical operations of the proposed Facility.

Par S. Mehta

Curriculum Vitae

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737 West Washington #2101
Chicago, IL 60661
312-493-3457
parmehta@hotmail.com

Office
Uropartners at the Glen
2600 Patriot Blvd Suite J
Glenview, IL
224-260-3100
pmehta@uropartners.com

Licensures

05/2004-Present	Illinois State Professional License
05/2004-Present	Illinois State Controlled Substance License
02/2007-Present	Federal DEA License

Certification

06/2007-present	Board Certification In Radiation Oncology The American Board Of Radiology

Positions

07/2007- 02/2013	Attending Physician, Rush Copley Medical Center Chair of Ancillary Services 2011-2013
03/2013-current	Medical Director at Uropartners at the Glen Attending physician in charge of a prostate specialized radiation oncology practice with an average of 60 daily external beam patients, prostate SBRT, 40 annual brachytherapy cases, Xofigo administrations, Pluvicto, 500 annual perirectal spacer placements (SpaceOAR, Barrigel, BioProtect), 100 annual transperineal prostate biopsies, Nanoknife IRE, and advanced prostate cancer treatment. Sub-I and PI Researcher Uropartners/Solaris 2614 Patriot Blvd, Unit A Glenview, IL 60026

Education and Training

07/2006–06/2007	Brachytherapy Fellowship Beth Israel Medical center, New York, NY
07/2002-06/2006	Resident- Radiation Oncology Rush University Medical Center, Chicago, IL

ATTACHMENT 11
Background of the Applicant

07/2001-06/2002	Intern- Rotating Rush University Medical Center, Chicago, IL
08/1996-05/2001	M.D./ M.B.A. University Of Illinois, Urbana, IL
08/1993-05/1996	B.S. Industrial and Operations Engineering University Of Michigan, Ann Arbor, MI
Professional Associations	ASTRO, ASCO, AMA, RSNA, ISMS, CRS, ABS
Research and Publications	• Huang J, LeVan P, Andre W, Wadhwa H, Tsambarlis P, Tauber D, Latchamsetty K, **Mehta P**, and Yonover PM. Absorbable Perirectal Hydrogel Spacer Injection to Reduce Rectal Dose in Low Dose Rate Prostate Brachytherapy. American Urologic Association, Engineering in Urology Poster Presentation, San Diego, May 2016. • Huang J, LeVan P, Andre W, Wadhwa H, Tsambarlis P, Tauber D, Latchamsetty K, **Mehta P**, and Yonover PM. Hydrogel Spacer ("SpaceOAR") in Image Guided Intensity Modulated Radiation Therapy for Prostate Cancer: A Single Institution Community-Based Experience. American Urologic Association, Engineering in Urology, Poster Presentation, San Diego, May 2016. • Organ and Function Preservation in Head and Neck Cancer – textbook chapter. Currently in progress, written with Dr. Louis Harrison. • Management of Non-melanoma Skin Cancer – textbook chapter. Currently in progress, written with Dr. Louis Harrison. • A Dosimetric Comparison of three-dimensional conformal, intensity-modulated radiation therapy, and MammoSite partial-breast irradiation. **Brachytherapy, Vol. 5, Issue 3, Jul-Sep 2006, pages 183-188.** Khan AJ, Kirk MC, **Mehta PS**, Seif NS, Griem KL, Bernard DA, Chu JC, Dickler A. • Split course radiotherapy with concurrent, cytotoxic chemotherapy for stage III non-small cell lung cancer: decreased acute and late toxicity without compromised efficacy. **Mehta PS**, Khan AJ, Zusag TW, Bonomi PD, Faber LP, Villafior V, Abrams RA. **Oral Presentation RSNA 2005. Manuscript submitted to Radiotherapy and Oncology.** • Is aggressive local-regional management warranted with oligometastatic non-small cell lung? Khan AJ, **Mehta PS**, Zusag TW, Bonomi PD , Faber LP, Abrams RA. **Manuscript accepted for publication in Radiotherapy and Oncology.** • Initial Clinical Results with the Mammosite Breast Brachytherapy Applicator in Women with Early-Stage Breast Cancer. Choo JJ, **Mehta PS**, Nguyen CN, Hasabou N, Schochet E, Gittleman MA, Henson R, Snider HC, Dowlatshahi K. **Abstract ASTRO 2005.** • A dosimetric analysis comparing an electron tumor bed boost with a tumor bed boost utilizing the Mammosite breast brachytherapy applicator. Kirk M, Dickler AD, **Mehta PS**, Khan AJ, Chu J, Griem KL, Nguyen C. **Abstract ASTRO 2005.** • A dosimetric comparison of 3D conformal, IMRT, and Mammosite partial

breast radiation. Dickler A, Kirk M, Khan AJ, **Mehta PS**, Chu J, Griem KL, and Nguyen C. **Abstract ASTRO 2005.**

- Clonogenic survival does not uniformly increase with split time between halves of 2-Gy fractions: implications for IMRT. Blazek ER, Khan AJ, **Mehta PS**, Foutch JL, Kirk MC, Chu J, Abrams RA. **Poster Radiation Research Society 2005.**
- Is Nodal Irradiation Necessary in Breast Cancer Patients with Positive Sentinel Node Biopsy Without Axillary Dissection? **IJROBP, Vol. 54, Issue 2, Supplement 1, 1 October 2002, pages 232-233.** Sarvi M, **Mehta P**, Vallow L, Dowlat K, Griem KL.

SpaceOAR Experience

- SpaceOAR Hydrogel Skills Workshop: Strategies and Techniques to Integrate SpaceOAR Hydrogel into Clinical Practice. American Urological Association Meeting, May 2019.
- SpaceOAR Center of Excellence Site since 2017.
  - Demonstrates best practices for SpaceOAR placement to new physician users and Boston Scientific employees.
  - Trained more than 100 physicians on SpaceOAR placement. Sharing clinical experiences and techniques.
- Performed more than 1500 SpaceOAR placements.
- Contributed to local TV news segment: Living Healthy Chicago-Uropartners and SpaceOAR Hydrogel. November 29, 2017.

May 21, 2026

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

Re: Advanced Radiation Center of Chicago, Certification and Authorization Letter

Dear Mr. Kniery,

As a representative of UroPartners, LLC and Solaris Health Holdings, LLC, I, Justin Cohen, M.D., 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 holds an interest in the UroPartners Surgery Center, LLC. Solaris Health Holdings, LLC has no ownership interest in any other healthcare facilities in Illinois. There have been no adverse actions in 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,

Justin Cohen, M.D.
President
UroPartners, LLC

ATTACHMENT 12
Purpose of the Project

This project involves the acquisition and installation of two major pieces of medical equipment. A Varian Ethos Machine (LINAC) and a SOMATOM go.Sim CT system from Siemens, to be utilized at the Advanced Radiation Center of Chicago located at 8915 West Golf Road, Niles, Illinois 60714. The Facility serves patients throughout northern Cook County, DuPage County, and southern Lake County (collectively, the "Service Area").

For purposes of this application, the geographic service area is defined as the communities within a 10-mile radius of the Facility, encompassing portions of northern Cook County and surrounding communities—a region with substantial population density and documented cancer incidence that supports demand for accessible, advanced radiation therapy services.

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

- **Varian Ethos Machine (LINAC):** This is an AI-driven, ring-mounted linear accelerator (LINAC) designed for fast, online adaptive radiotherapy (OART). It enables clinicians to adjust treatment plans in real time based on daily anatomical changes, delivering personalized and precise radiation in approximately 15 minutes. The Varian Ethos LINAC is recognized for mitigating the loss of healthy tissue during radiation treatment of tumors.
- **SOMATOM go.Sim from Siemens System:** This system is a 64-slice CT scanner designed specifically for radiation therapy simulation, featuring an 85 cm bore for universal patient comfort and optimal positioning. The machine utilizes AI-driven DirectORGANS contouring for automated organ-at-risk (OAR) delineation to standardize and accelerate the simulation process.

Existing Problem and Need for Equipment Replacement

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 equipment being rendered unusable. The current LINAC at the Facility is approaching the end of its functional lifespan, and continued reliance on aging technology presents an increasing risk of unplanned service disruption for the thousands of patients who depend on the Facility for life-saving radiation treatments.

The acquisition of a new LINAC and CT system serves the dual purpose of (1) ensuring continuity of access to essential radiation therapy services and (2) advancing the quality of care available to the patient population by introducing adaptive radiation therapy capabilities. This approach promotes efficient health planning by allowing the Advanced Radiation Center of Chicago to gradually phase out its existing machine while bringing the new equipment up to full utilization, thereby avoiding any gap in patient services.

Improving Health Services: Adaptive Radiation Therapy

The Varian Ethos system represents a fundamental advancement in radiation oncology that directly improves patient care and well-being. Unlike conventional radiation therapy, which relies on a single pre-treatment plan delivered across all treatment sessions, the Ethos system enables daily adaptive treatment planning. Each fraction can be re-optimized based on the patient's anatomy of the day, shifting radiation therapy from a static "plan-and-deliver" model to a continuously optimized, patient-specific therapeutic process.

ATTACHMENT 12
Purpose of the Project

The clinical benefits of this approach include:

- Daily adaptive treatment planning that accounts for physiologic variability such as weight changes, bladder filling, rectal gas, and tumor shrinkage across the course of therapy.
- AI-driven contouring and dose recalculation that allow clinicians to tailor radiation precisely to tumor position and shape changes in real time.
- Improved organ-at-risk protection, as surrounding normal tissues (bladder, rectum, bowel) are re-evaluated daily, enabling tighter sparing and reduced toxicity.
- The potential for planning target volume (PTV) margin reduction, which decreases radiation exposure to healthy tissue.
- On-table decision-making that enables physicians to review and approve multiple plan options during treatment, providing true point-of-care personalization.
- Workflow integration of AI and imaging that combines cone-beam CT imaging with automated segmentation and rapid dose calculation to support adaptive workflows without excessive treatment delays.

This technology is particularly beneficial for patients with prostate cancer, pancreatic cancer, breast cancer, lung cancer, head and neck cancer, and metastatic disease—conditions that represent a significant portion of cancer diagnoses within the Service Area.

Prostate and Pelvic Cancer Radiation Therapy

Prostate cancer is the most common non-skin cancer in the United States. The Prostate Cancer Foundation reports that 1 out of every 8 men will be diagnosed with prostate cancer in their lifetime, with routine screening typically beginning at age 50. According to the Illinois Department of Public Health, African Americans and Latinos account for almost 60% of patient deaths due to prostate cancer in Illinois—a statistic of particular relevance given the demographic composition of the Service Area.

Radiation therapy is a primary modality for curative treatment of localized prostate disease, and ensuring continued access to advanced radiation therapy services is essential to maintaining timely care for this large and clinically significant patient population. This project aims to maintain and enhance treatment capacity for prostate cancer and other pelvic malignancies.

Modern adaptive radiation therapy systems further strengthen treatment options by accounting for day-to-day anatomical variability in pelvic organs. Online adaptive radiotherapy allows clinicians to modify treatment plans in real time based on daily imaging and anatomical changes. This approach is specifically designed to improve target coverage and reduce radiation exposure to adjacent organs at risk, such as the bladder and rectum.

Clinical evidence reinforces the value of these capabilities. A retrospective study of prostate cancer patients treated with the Varian Ethos system found that adaptive plans achieved target coverage benchmarks in 418 out of 422 treatment fractions, significantly outperforming non-adaptive plans. These findings demonstrate improved consistency and reliability in treatment delivery, which is particularly important in pelvic cancers where small anatomical changes can impact dose distribution.

ATTACHMENT 12
Purpose of the Project

Radiation Treatment for Additional Malignancies

In addition to prostate cancer, this project supports comprehensive radiation oncology capabilities for a broad range of malignancies. External beam radiation therapy is a well-established treatment tool for bladder cancer and is frequently incorporated into bladder-preserving treatment strategies. These approaches combine radiation with other therapies to achieve oncologic outcomes comparable to surgery in selected patients while avoiding more invasive procedures.

The new LINAC system will also enable the Facility to provide stereotactic body radiation therapy (SBRT) for renal cell carcinoma in select patients. Clinical guidelines and systematic reviews describe SBRT as an effective option for patients who are medically inoperable or have contraindications to surgery, expanding treatment accessibility for this population.

Radiation therapy further plays a role in the management of less common urologic malignancies, including penile cancer, where external beam radiation and other modalities may offer organ-preserving treatment options in appropriately selected patients. The increased precision of the Ethos system is also beneficial for developing treatment strategies for complex cases involving abdominal tumors where inter-fraction motion is significant.

By supporting treatment across this spectrum of cancers, the project ensures that patients within the Service Area have continued access to a full range of evidence-supported radiation therapy options, reducing the need to travel outside the region for specialized care.

CT Imaging and Simulation for Treatment Planning and Urologic Evaluation

The SOMATOM go.Sim system fulfills a critical function in the radiation therapy process by enabling precise CT-based simulation for treatment planning. Patients undergoing radiation therapy require CT imaging to define tumor volumes and surrounding anatomy, which forms the basis for accurate dose calculation and treatment delivery.

Beyond treatment planning, CT imaging is widely recognized as an essential diagnostic tool for evaluating urologic conditions that frequently present in clinical practice. CT is the primary imaging modality for assessing a variety of urinary tract diseases, including renal tumors, bladder carcinoma staging, and evaluation of hematuria. CT urography is described as highly accurate for detecting upper tract urothelial malignancies, underscoring its importance in cancer detection and staging.

Addressing Regional Need and Ensuring Continuity of Care

A fundamental purpose of this project is to ensure uninterrupted access to essential oncology services as existing equipment approaches the end of its functional lifespan. By proactively replacing aging technology, the project minimizes the risk of service disruption and supports continuity of care for patients who require timely radiation therapy.

ATTACHMENT 12
Purpose of the Project

The project also addresses geographic gaps in access to advanced radiation modalities within the northern Chicago suburban region. Adaptive radiation therapy capabilities remain limited outside of major urban academic medical centers in downtown Chicago, and the proposed equipment will expand access to these advanced treatment options for patients residing in the surrounding suburban communities. Without this project, patients in the Service Area who could benefit from adaptive radiation therapy would be required to travel to downtown Chicago or other distant facilities, creating barriers related to transportation, time, and cost that may delay or deter treatment.

This need is further supported by statewide cancer surveillance data. The Illinois State Cancer Registry serves as the population-based source for cancer incidence information in Illinois and provides essential data used to inform health planning and resource allocation. State-level data demonstrate that urologic cancers, including prostate and bladder cancer, remain an ongoing concern for Illinois residents, with documented incidence rates over recent multi-year periods. These data reinforce the importance of maintaining accessible, high-quality radiation therapy services within the Service Area.

A primary objective of this project is to ensure continuity of radiation therapy services for the existing patient population without interruption. The Applicants intend to complete installation and commissioning of the Varian Ethos LINAC and SOMATOM go.Sim CT system within 12 months of CON approval. All active radiation therapy patients will be transitioned from the existing equipment to the new LINAC with zero interruption in scheduled treatment courses, and current patient volume capacity, as measured by treatment fractions delivered per month, will be maintained throughout the equipment transition period.

The project will also expand access to adaptive radiation therapy within the Service Area. Online adaptive radiation therapy (OART) will be offered to clinically appropriate patients within 90 days of equipment commissioning, with a target of achieving utilization of adaptive treatment protocols for at least 40% of eligible prostate and pelvic cancer patients within 24 months of commissioning. By making this advanced modality available locally, the project will reduce the proportion of Service Area patients who must travel to downtown Chicago or other distant facilities for adaptive radiation therapy.

Finally, the project is designed to improve clinical outcomes and reduce treatment-related toxicity over time. The Facility will target achievement of planning target volume dose conformity benchmarks in at least 95% of adaptive treatment fractions within the first 24 months of operation.

References:

1. The Prostate Cancer Foundation. Understanding Prostate Cancer. https://www.pcf.org/patient-support/understanding-prostate-cancer/.
2. Malygina, H., Salazar Zuniga, B., Auerbach, H., Ries, M., Dzierma, Y., Hecht, M., & Palm, J. (2025). Daily online adaptation enhances target coverage in prostate cancer radiotherapy: a retrospective analysis. Frontiers in oncology, 15, 1662671. https://pmc.ncbi.nlm.nih.gov/articles/PMC12620223/.
3. Martingano, P.; Cavallaro, M.F.M.; Bozzato, A.M.; Baratella, E.; Cova, M.A. CT Urography Findings of Upper Urinary Tract Carcinoma and Its Mimickers: A Pictorial Review. Medicina 2020, 56, 705. https://www.mdpi.com/1648-9144/56/12/705.
4. Lakhvir Kaur et al. MRI-Linac radiation therapy outcomes in patients with prostate, breast and other advanced malignancies.. J Clin Oncol 42, e13811-e13811(2024). https://ascopubs.org/doi/pdf/10.1200/JCO.2024.42.16_suppl.e13811.
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ATTACHMENT 12
Purpose of the Project

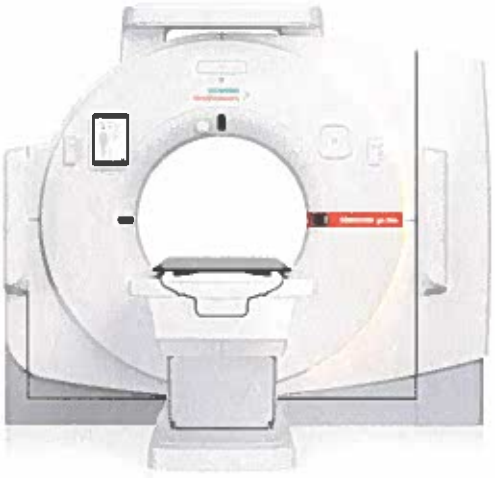
Varian Ethos Machine (LINAC)

The Varian Ethos system is an AI-driven adaptive radiotherapy solution designed to optimize treatment planning and delivery for both adaptive and conventional workflows. It provides a patient-tailored approach, allowing clinicians to choose the best treatment option while using efficient technologies and guided workflows to support decision making. The system also providers to leverage different treatment techniques such as IGRT, IMRT, VMAT, and SBRT, and can incorporate MR, PET, and CT imaging throughout planning and treatment.

In addition, Ethos integrates advanced imaging with AI planning and segmentation to improve precision, efficiency, and confidence in treatment delivery. It enables clinicians to visualize patient anatomy, respond to anatomical changes, and calculate dose directly from imaging to support adaptive radiotherapy. The system also enhances clinical and operational performance through streamlined workflows, data integration, and unified management of treatments across platforms.

ATTACHMENT 12
Purpose of the Project

SOMATOM go.Sim CT System



The SOMATOM go.Sim is a dedicated CT simulator for radiation therapy that combines hardware and software into a single, integrated system to streamline the entire CT simulation process. It is designed to reduce errors caused by complex workflows and manual data handling by using automation and intelligent features. This integration helps create a more efficient, reproducible workflow, shortens the time to treatment, and allows staff to focus more on patient care while improving consistency in simulation results.

The system enhances treatment planning by providing optimized image quality for tumor delineation and supporting advanced functions such as AI-based auto-contouring, which helps reduce variability in planning. It also simplifies tasks with a user-friendly design and coordinated workflow tools that improve accuracy and productivity. Overall, SOMATOM go.Sim is built to deliver precise imaging, faster and more reliable workflows, and a more patient-centered radiotherapy simulation process.

ATTACHMENT 12
Purpose of the Project

Understanding Prostate Cancer

What is Prostate Cancer?

In general, cancer is a condition in which a normal cell becomes abnormal and starts to grow uncontrollably without having the signals or "brakes" that stop typical cell growth. The prostate is a small gland located below the bladder that is responsible for secreting one of the components of semen.

Prostate cancer occurs when a normal prostate cell becomes altered and starts growing in an uncontrolled way. Prostate cancer cells form masses of abnormal cells known as tumors.

How Common is Prostate Cancer?

Approximately one in eight men in the U.S. will be diagnosed with prostate cancer in his lifetime, about the same rate as breast cancer in women. For African American men, the rate is one in six. Prostate cancer is the second most common type of cancer in men, after skin cancer. In 2026, about 333,830 new cases of prostate cancer will be diagnosed in the U.S., and about 36,320 patients will die of the disease. Worldwide, more than 1.4 million men are diagnosed each year.

Learn more about potential symptoms of prostate

ATTACHMENT 12
Purpose of the Project

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Daily online adaptation enhances target coverage in prostate cancer radiotherapy: a retrospective analysis

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Abstract

Introduction

Online adaptive radiotherapy aims to improve treatment quality by accounting for inter-fractional variation in anatomy. This study presents a quantitative comparison between adapted and non-adapted scheduled plans with identical margins in a real-world clinical setting.

Methods

We retrospectively analyzed 422 fractions from 43 patients with prostate cancer treated with the Varian Ethos system. All patients received hypofractionated treatment with 3 Gy per fraction up to a cumulative dose of 60 Gy. For each fraction, the scheduled plan (planned on planning CT, calculated on synthetic CT derived from daily cone beam CT) was compared to the adapted plan

(planned and calculated on actual daily anatomy) by means of several dose-volume metrics. Comparative statistics regarding dose-volume metrics were performed using Wilcoxon signed-rank test for paired data with a two-sided hypothesis.

Results

Adapted plans delivered significantly better target coverage, conformality, and homo-geneity than scheduled plans. The constraints D95% ≥ 95% and V95% ≥ 95% were met in 418 out of 422 fractions with the adapted plan, compared to only 41%-84% of fractions with the scheduled plan. Median absolute improvements for these metrics ranged between 1.5 and 6.0 percentage points. Most organ-at-risk metrics remained unchanged or showed only minor differences. Interquartile ranges decreased across all metrics.

Conclusions

Adaptation significantly improved target dose metrics compared to non-adapted plans, without compromising organs-at-risk sparing. Interquartile ranges were reduced for all metrics evidencing better repeatability of adapted plans.

Keywords: prostate cancer, online adaptive radiotherapy (oART), Varian Ethos, dosimetric impact, dosimetric distribution, organs-at-risk sparing, CBCT

1. Introduction

Prostate cancer is among the most common malignancies affecting men worldwide [1, 2], and radiotherapy (RT) remains one of its cornerstone treatment modalities. However, daily anatomical variations—particularly in bladder and rectal filling—pose a significant challenge to accurate dose delivery. Such interfractional changes can lead to undercoverage of the prostate target and unintended dose escalation to surrounding organs at risk (OARs), thereby compromising tumor control and increasing the risk of treatment-related toxicity [3, 4].

Online adaptive radiotherapy (oART) has emerged to address these challenges by enabling real-time modification of the treatment plan based on each day's patient anatomy. By acquiring a cone-beam CT (CBCT) on each treatment day, re-segmenting targets and OARs, and re-optimizing the dose distribution, oART can substantially mitigate the effects of anatomical variability and enhance treatment precision.

ATTACHMENT 12
Purpose of the Project

The Varian Ethos system (Varian Medical Systems, Palo Alto, CA, USA) (5) integrates daily CBCT imaging with artificial-intelligence-driven auto-segmentation and fully automated plan re-optimization, creating a seamless workflow for oART in routine clinical practice. This capability is particularly valuable in the management of prostate cancer, where bladder and rectal filling can induce significant prostate motion. In hypofractionated regimens—where each fraction delivers a high dose per session—such precision is critical. Daily adaptation not only improves target coverage but also holds the promise of reducing toxicity to the bladder, rectum, and other pelvic structures.

Several studies have shown dosimetric benefits of adaptation for a limited number of patients (partially with simulated data) for different prostate cases: prostate stereotactic body radiation therapy (6), prostate bed (7), prostatic fossa (8), and prostate and seminal vesicles (9). The advantages of oART were also reported for gynecological (10), rectal (11), bladder (12, 13), and other cancers. In this study, we present a large and consistent cohort of 40 prostate cancer patients who underwent oART using the Varian Ethos system with a double simultaneous integrated boost (SIB) technique at our department.

2. Method and materials

2.1. Online adaptive radiotherapy workflow

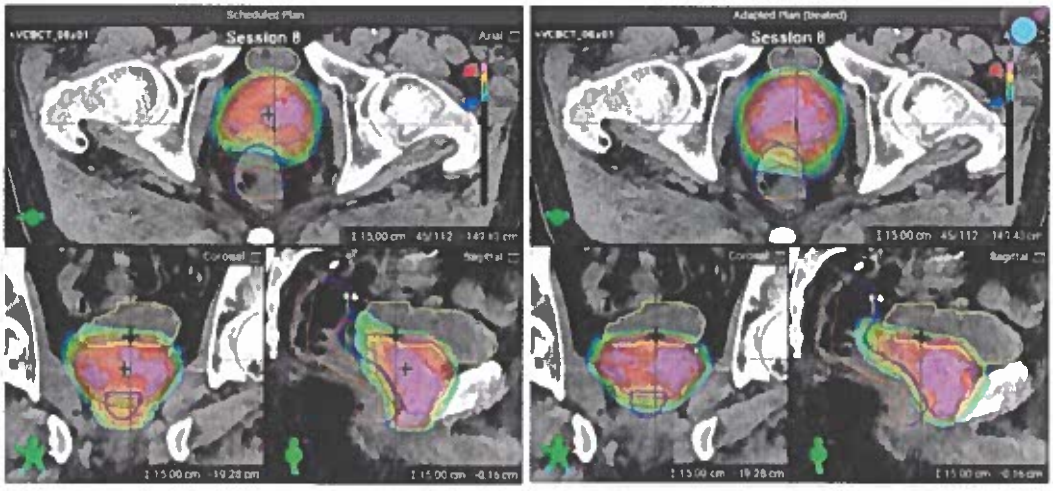
CBCT-based oART using the Varian Ethos system is conducted with a pre-defined workflow. The process begins with the planning CT (pCT), where the treatment intent—including dose prescription, planning objectives, and delineation of OARs—is established.

A reference treatment plan is generated on the planning CT using one of several predefined beam configurations: intensity-modulated radiotherapy (IMRT) with 7, 9, or 12 equidistant fields, or volumetric modulated arc therapy (VMAT) with two or three arcs. Once this reference plan is approved, it becomes available for daily treatment. Our early clinical experience indicated that VMAT plan calculation required considerably more time while offering only marginal dosimetric benefit compared with IMRT. For this reason, VMAT plans (Ethos 1.0) were not used in routine clinical practice at our institution.

At each treatment session, the patient is positioned and a CBCT scan is acquired. Following a quality check of the image, the system automatically propagates the planning contours to the CBCT of the day. These propagated contours must then be reviewed and, if necessary, edited by the

user. Using deformable image registration, the CBCT anatomy is mapped back to the planning CT to preserve Hounsfield unit accuracy (synthetic CT). On this basis, two dose distributions are calculated: (1) the dose from the scheduled (non-adapted) plan applied to the current anatomy, and (2) a newly re-optimized adapted plan, generated using the original treatment intent and constraints, tailored to the anatomy of the day (Figure 1).

Figure 1.



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Scheduled and adapted plans on a CBCT image for the same treatment session. Left panel: The scheduled plan. Right panel: The adapted plan. The color scheme for the contours: bladder – yellow, rectum – dark blue, PRW – orange, PTV/SIB1/SIB2 – red/green/blue. The dose distributions are visualized using a color wash, where blue corresponds to 2.28 Gy and red to 3 Gy. Doses above 3 Gy are indicated in pink. The scheduled plan shows strong underdosage for PTV and SIB1 which could be compensated with the adapted plan, as can be seen in sagittal and axial views.

The clinician then compares both plans and selects the one to be delivered. In practice, the adapted plan typically offers superior dosimetric quality, and at our institution it is selected in > 99% of sessions for treatment.

2.2. Treatment characteristics

Between July 2023 and October 2024, a total of 72 patients were treated with the Ethos system at our institution. The majority of patients underwent pelvic radiotherapy, primarily for prostate cancer. Patients with primary prostate cancer radiotherapy are treated at our institution with the in-house protocol based on the CHHiP trial (14).

For this *post-hoc* analysis, we selected all patients with a confirmed diagnosis of prostate cancer, who were treated with the 2 SIBs concept at our institution and whose data could be fully exported from the Ethos system. These 49 patients had been treated prior to the commencement of this study, making this an exploratory analysis.

Planning target volume (PTV), SIB1, and SIB2 are structures derived from prostate and seminal vesicles contours, which is necessary for the adaptive treatment workflow since they will be automatically generated by the system based on the adapted prostate and seminal vesicle contours. SIB2 is defined as the prostate with 3 mm margins (posteriorly 0 mm). SIB1 includes the prostate and the proximal 1 cm of the seminal vesicles with 6 mm margins (posteriorly 3 mm). PTV is defined the same as SIB1 but includes the proximal 2 cm of the seminal vesicles with 6 mm margins in all directions including posterior. The cumulative prescribed doses for PTV, SIB1, and SIB2 are respectively 48 Gy, 57.6 Gy, and 60 Gy.

Dose objectives for OARs in this study were aligned with our institution's in-house protocol (15), which is based on the guidelines from the CHHiP (14), PROFIT (16), PACE-B (17), and PACE-C (18) trials. In our institution, a posterior rectum wall (PRW) is used as an additional OAR (reasoning and PRW contouring have been described previously (19)).

To ensure better bladder sparing, the patients are instructed to follow our in-house "Bladder and bowel preparation instructions" (15), which aim at a reproducibly empty rectum and a comfortably full bladder.

2.3. Patient selection

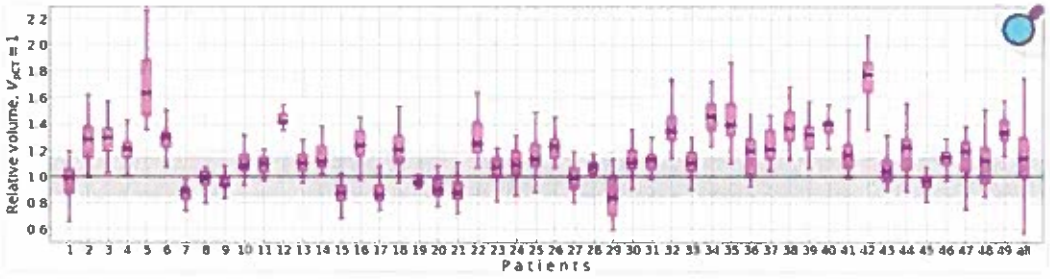
As previously discussed (19), a systematic bias exists in which prostate contours on the pCT tend to be smaller than those on CBCT. This discrepancy does not indicate an error but arises from the ESTRO ACROP contouring guidelines (20), which recommend assuming equal levator ani muscle thickness adjacent to the prostate and rectum on CT, while on MRI (magnetic resonance imaging)

these structures can be clearly distinguished. Consequently, MRI-based contouring yields smaller target volumes by avoiding unnecessary inclusion of the levator ani muscles. In CT-only workflows, the Santorini plexus is also frequently included due to limited soft-tissue contrast, further enlarging prostate, CTV, and PTV volumes.

At our institution, MRI is used to support pCT contouring but is not always referenced during adaptive workflows, occasionally leading to larger prostate contours in adapted datasets. Large discrepancies between the prostate contour volume on the pCT (used for the scheduled plan) and on the CBCT (used for the adapted plan) can introduce artifacts in dosimetric comparison (19).

To minimize variability and enhance data homogeneity, we applied a threshold of 15% to the prostate volume for each session: $\Delta V = |V_{prostate,pCT} - V_{prostate,CBCT}| \leq 15\%$. This threshold allows to homogenize the data while accounting for physiological prostate swelling often observed during the radiotherapy (21). Fractions exceeding this threshold were excluded, resulting in the removal of 555 out of 980 fractions due to pronounced contour discrepancies (see Figure 2 for prostate volume distributions). The excluded fractions were analyzed separately. Consequently, six patients were entirely excluded from the study.

Figure 2.



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Relative prostate volume on CBCTs (V_{CBCT}/V_{pCT}) for each patient. The gray area marks the allowed prostate volumes for a fraction to be included in the study.

Additionally, three interrupted sessions were excluded. The final dataset comprised 422 fractions (ranging from 1 to 20 fractions per patient) from a total of 43 patients, providing a consistent basis for analysis. Among these 422 fractions, the scheduled plan was selected for treatment in only three sessions.

2.4. Data analysis

Since this is a retrospective study, all data was available prior to the beginning of the study. Dose and structure DICOM files were exported from the Ethos system. Dose-volume histograms were computed using a custom-developed Python script based on the dicompyler-core package (version 0.5.6) (22).

For each dose-volume metric, we calculated the difference between the metric value obtained with the scheduled plan and that obtained with the adapted plan for each fraction. To assess the significance of these differences, we applied the Wilcoxon signed-rank test for paired data with a two-sided alternative hypothesis.

Additionally, we evaluated the homogeneity index $HI = (D1\% - D99\%)/D_{prescribed}$ (23) for SIB2 as well as the conformation number $CN = TV95\%/TV \times TV95\%/V95\%$ for PTV, where $TV95\%$ and $V95\%$ are respectively the volume of PTV and the volume of tissue covered by 95% of the PTV prescribed dose, TV is the total volume of PTV (24). The CN quantifies both the target coverage (the first term of the formula) and the healthy tissue sparing (the second term).

To estimate both the central tendency and dispersion of non-normally distributed data, we calculated the Hodges-Lehmann median along with the corresponding quartiles (Q1 and Q3).

A custom Python script was developed for this analysis, utilizing core libraries such as NumPy, SciPy, and statistics. Given the exploratory nature of this study, p-values are considered descriptive, with $p<0.05$ interpreted as indicative of statistical significance. No Bonferroni correction was applied; instead, we always present an absolute p-value if $p \geq 0.001$.

3. Results

3.1. Patient characteristics

ATTACHMENT 12
Purpose of the Project

A total of 43 patients (Table 1) with a confirmed diagnosis of prostate cancer were included in this study. Clinical staging revealed that 24 patients (55.8%) had T1 tumors, 18 (41.9%) had T2 tumors, and 1 patient (2.3%) was classified as T3. Androgen deprivation therapy was administered to 17 patients, depending on clinical indications and risk stratification. Adaptive radiotherapy was delivered in most cases using IMRT techniques. Most patients received either 9-beam or 12-beam IMRT; four patients were treated with different IMRT beam arrangements in different sessions, and one patient received either VMAT or IMRT, although all VMAT-treated fractions were excluded by the prostate-volume criterion.

ATTACHMENT 12
Purpose of the Project

Table 1.

Demographic characteristics including age, NCCN (National Comprehensive Cancer Network) risk group, Gleason and ISUP (International Society of Urological Pathology) grades, cancer stage, receiving of the androgen deprivation therapy, the latest lPSA value before or shortly after the start of the treatment, as well as the plan modality.

Age, years	**Mean**	**Min - max**
	72.3	55 - 83
NCCN riskgroup	**# of patients**	**% of patients**
Low	12	27.9
Intermediate	27	62.8
High	4	9.3
Gleason (ISUP) grade	**# of patients**	**% of patients**
6 (1)	12	27.9
7a (2)	18	41.9
7b (3)	9	20.9
8 (4)	3	7.0
Cancer stage	**# of patients**	**% of patients**
T1b	1	2.3
T1c	23	53.5
T2a	2	4.7
T2b	2	4.7
T2c	14	32.6
T3	1	2.3
	# of patients	**% of patients**
Androgendeprivation therapy	17	39.5
lPSA, ng/ml	**Mean**	**min - max**
	6	0.08 - 27

Plan	# of patients	% of patients
IMRT 09	12	27.9
IMRT 12	26	60.5
Combination	5	11.6

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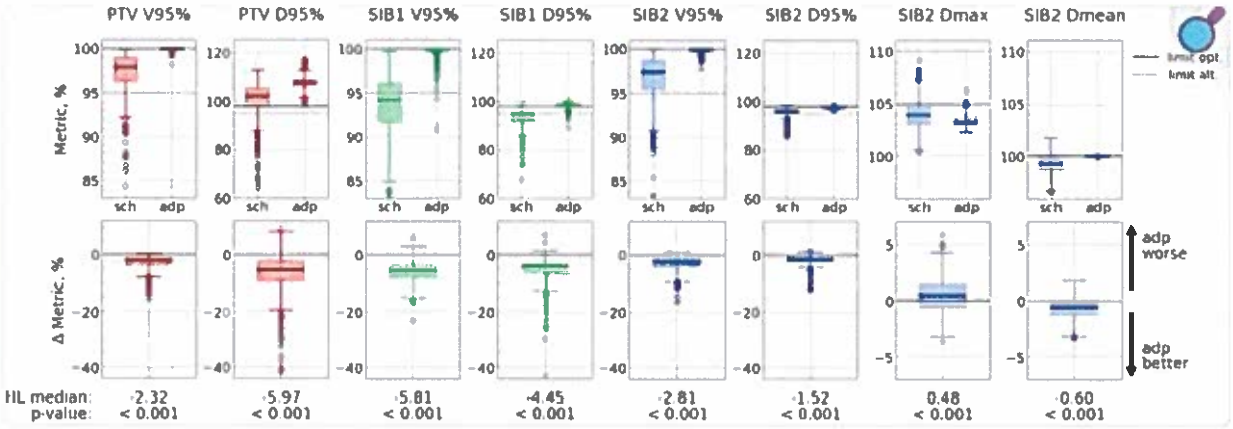
Some patients received different plan modalities in different sessions (represented by "Combination").

3.2. Target metrics

Adaptation significantly enhanced target coverage as measured by D95% (p<0.001) for all targets, with the improvement ranging from 1.5 to 6.0%. (Hereafter, we estimate metric changes in terms of Hodges-Lehmann median of the difference distributions, all values refer to absolute dose changes, e.g. percentage points.) Additionally, V95% increased on average by 2.3 to 5.8% (Figure 3 ; Supplementary Table S1 in the Supplementary Material). Furthermore, the interquartile range (IQR = Q3 - Q1) decreased with adaptation for all target metrics.

Figure 3.



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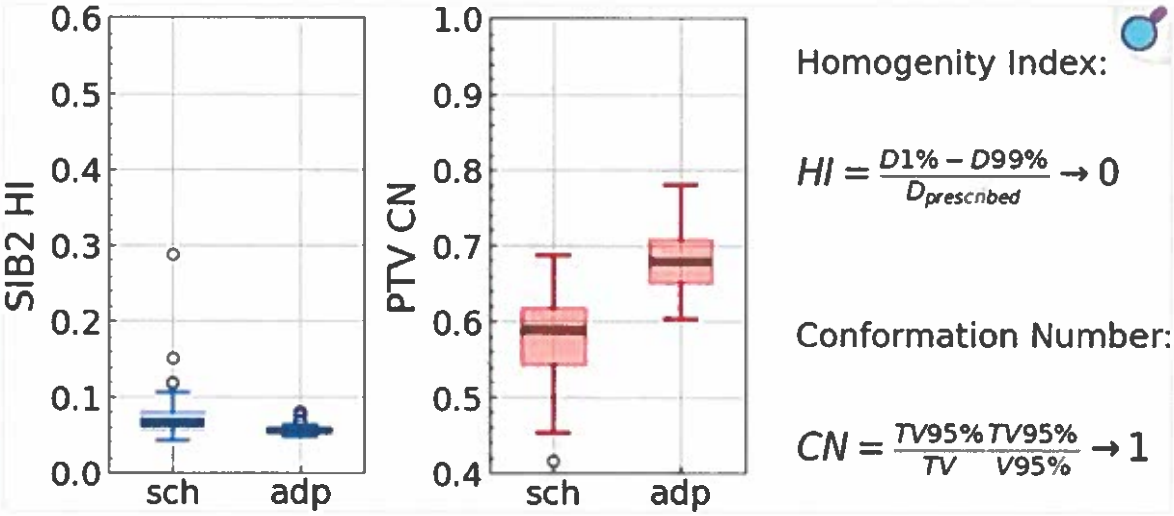
Target metric distributions for scheduled ("sch") and adapted ("adp") plans (top panel), and distributions of difference: $metric_{sch} - metric_{adp}$ (bottom panel). Each vertical pair of subplots corresponds to a single metric. Solid lines correspond to optimal limits for each metric, and dotted lines – to alternative ones (top panel). Hodges-Lehmann median for each difference distribution is given under the corresponding subplot, as well as the *p*-value from the corresponding Wilcoxon test. The labels "adp better" and "adp worse" are valid for all metrics except SIB2 Dmax.

The adapted plan demonstrated markedly improved homogeneity and conformality (Figure 4). Specifically, the homogeneity for SIB2 (ideal value of 0) improved from 0.092[0.080, 0.115] (Hodges-Lehmann median [Q1, Q3]) to 0.056[0.054, 0.059] ($p<0.001$), with its maximum value decreasing from 0.75 to 0.11. The conformation number for PTV (ideal value of 1) increased from 0.66[0.64, 0.68] to 0.685[0.671, 0.699] ($p<0.001$), with its minimum value increasing from 0.53 to 0.62.

Figure 4.



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Homogeneity index for SIB2, as well as conformation number for PTV for all 422 fractions for scheduled ("sch") and adapted ("adp") plans. The right panel presents the definitions and the ideal values for the indices.

For the adapted plan, all alternative target constraints (except SIB2 Dmean) were satisfied in 418 out of 422 fractions: $D95\% \geq 95\%$ and $V95\% \geq 95\%$. Only in four fractions did both SIB1 constraints fail, while those for SIB2 and PTV were consistently met (Table 2).

Table 2.

The percentage of fractions with satisfied alternative goal (which is equal to the optimal goal for some metrics) for each metric for three categories of the prostate contour volume on CBCT scan: 1. much smaller than on pCT: $V < 0.85V_{pCT}$; 2. within the selected threshold (e.g. included into the main analysis); 3. much bigger than on pCT: $V > 1.15V_{pCT}$.

Metric and alternative goal		Percentage of fractions with satisfied alternative goal					
		With scheduled plan			With adapted plan		
		$V < 0.85V_{pCT}$	$0.85–1.15V_{pCT}$	$V > 1.15V_{pCT}$	$V < 0.85V_{pCT}$	$0.85–1.15V_{pCT}$	$V > 1.15V_{pCT}$
PTV	V95% ≥ 95%	91.4	84.4	49.1	100.0	100.0	100.0
PTV	V95% ≥ 95%	91.4	84.4	48.9	100.0	100.0	100.0
SIB1	V95% ≥ 95%	85.7	40.8	2.3	97.1	99.1	99.8
SIB1	D95% ≥ 95%	85.7	40.8	2.3	97.1	99.1	99.8
SIB2	V95% ≥ 95%	97.1	80.6	24.3	100.0	100.0	100.0
SIB2	D95% ≥ 95%	97.1	80.6	24.3	100.0	100.0	100.0
SIB2	Dmean≥ 100%	25.7	27.3	8.5	42.9	65.6	69.7
SIB2	Dmax ≤ 110%	100.0	100.0	99.8	100.0	100.0	100.0
Bladder	V60Gy < 5%	88.6	87.2	90.9	98.6	97.6	94.8
Bladder	V48Gy < 25%	78.6	91.2	95.7	97.1	97.9	95.7

ATTACHMENT 12
Purpose of the Project

Metric and alternative goal		Percentage of fractions with satisfied alternative goal					
		With scheduled plan			With adapted plan		
		$V < 0.85V$ pCT	$0.85–1.15V$ pCT	$V > 1.15V$ pCT	$V < 0.85V$ pCT	$0.85–1.15V$ pCT	$V > 1.15V$ pCT
Bladder	V40Gy < 50%	95.7	99.3	99.2	100.0	99.5	99.2
Rectum	V56Gy < 25%	100.0	100.0	100.0	100.0	100.0	100.0
Rectum	V52Gy < 30%	100.0	100.0	100.0	100.0	100.0	100.0
Rectum	V48Gy < 35%	100.0	100.0	100.0	100.0	100.0	100.0
Rectum	V40Gy < 50%	100.0	100.0	100.0	100.0	100.0	100.0
Rectum	V32Gy < 51%	92.9	97.2	99.2	100.0	100.0	100.0
Rectum	V24Gy < 70%	97.1	96.7	95.3	100.0	100.0	99.8
PRW	V37Gy < 5%	84.3	86.0	93.8	100.0	98.8	99.6
PRW	Dmax < 2.1 Gy	52.9	69.2	84.1	91.4	92.4	97.1
Bowel	V48Gy < 6 ccm	25.7	33.4	26.2	27.1	32.9	29.9
Bowel	V40Gy < 17 ccm	42.9	43.6	34.4	38.6	41.7	37.7
Bowel	Dmax < 2.6 Gy	92.9	89.1	91.5	94.3	90.0	91.3

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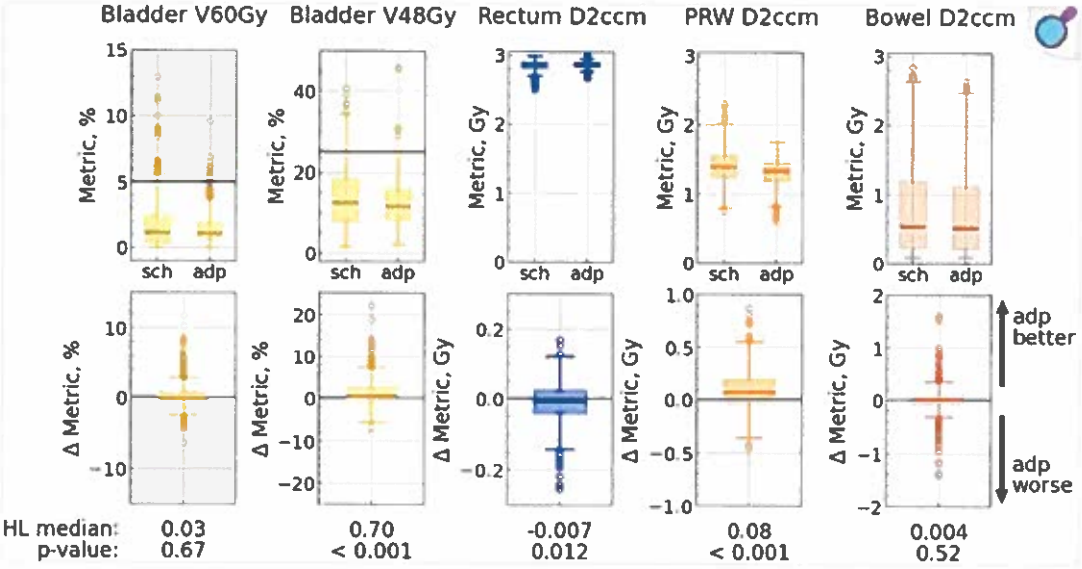
3.3. OAR metrics

Bladder V60Gy remained unchanged with adaptation, whereas V48Gy and V40Gy exhibited modest but statistically significant ($p < 0.001$) improvements (Figure 5; Supplementary Table S1 in the Supplementary Material). The percentage of fractions meeting the optimal constraints for the bladder metrics was higher with the adapted plan than with the scheduled one, and was ranging between 97.6% and 99.5% (Table 2).

Figure 5.



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OAR metric distributions for scheduled ("sch") and adapted ("adp") plans (top panel), and distributions of difference: $metric_{sch} - metric_{adp}$ (bottom panel). Each pair of subplots corresponds to a single metric. Solid lines correspond to optimal limits for each metric (top panel). Hodges-Lehmann median for each difference distribution is given under the corresponding subplot, as well as the *p*-value from the corresponding Wilcoxon test.

Among the evaluated rectum metrics (V56Gy, V52Gy, V48Gy, V40Gy, V32Gy, V24Gy, D2ccm), five showed statistically significant changes: the first four metrics experienced a slight deterioration (less than 0.8%) with adaptation, while V24Gy showed a minor improvement. Nevertheless, the adapted plan met all optimal rectum constraints in all fractions (Table 2 ; Supplementary Table S1 in the Supplementary Material).

Furthermore, the adapted plan outperformed the scheduled plan in terms of the PRW metrics: the dose to 2 ccm decreased by 0.08 Gy, the maximum dose was reduced by 0.17 Gy, and V37Gy improved by 0.65% (in all three cases $p<0.001$), while the percentage of fractions meeting the optimal constraint increased for V37Gy from 86% (with the scheduled plan) to 99% (with the adapted one), and for Dmax from 69% to 92% (Table 2 ; Supplementary Table S1 in the Supplementary Material).

The IQR decreased with adaptation for all bladder, rectum, and PRW metrics.

Bowel metrics did not exhibit any significant differences with adaptation.

3.4. Excluded sessions

When the prostate contour on CBCT exceeded the 15% threshold (e.g. a bigger prostate on CBCT, 485 sessions), median reductions in the target metrics D95% and V95% ranged from 4.5% to 14.9% (Supplementary Figure S1 in the Supplementary Material). The scheduled plan could not account for such a big prostate on the daily CBCT satisfying the goals for these target metrics in much fewer sessions in comparison with the adapted plan (see Table 2). For the sessions with a smaller prostate on CBCT (70 sessions), the adapted plan still conferred statistically significant dosimetric improvements over the scheduled plan, although the magnitude of benefit was reduced (between 0.8% and 2.3%) relative to the cases with a prostate volume close to V_{pCT} (Supplementary Figure S2 in the Supplementary Material). The scheduled plan could also fulfill the goals in the most sessions.

Moreover, an enlarged prostate contour on CBCT (and hence larger targets) artificially favored the scheduled plan for OAR metrics—they appeared slightly lower than with adaptation (Supplementary Figure S1 in the Supplementary Material), whereas the converse held true for a smaller prostate contour (Supplementary Figure S2 in the Supplementary Material).

4. Discussion

ATTACHMENT 12
Purpose of the Project

To enable an unbiased comparison between scheduled and adapted plans, we applied a strict exclusion criterion based on prostate contour volume. The rationale for this approach was to avoid artifacts that arise when the prostate contour on the CBCT deviates substantially from that on the planning CT (19). The main reason for this deviation is the availability of MRI fusion for the planning CT but the lack of MRI fusion for daily CBCTs during adaptive sessions. This aspect combined with the ESTRO ACROP contouring guidelines (20), can introduce contouring bias. Naturally, MRI-guided radiotherapy can largely eliminate this issue by providing consistent MRI-based contours for all fractions.

We observed the following artifacts when the prostate appeared larger on CBCT (see columns "$V > 1.15V_{pCT}$" in Table 2 ; Supplementary Figure S1 in the Supplementary Material):

1. The scheduled plan on CBCT, evaluated using the adapted contours, appears to provide poorer target coverage even in the absence of anatomical changes. This occurs simply because the apparently larger CTV/PTV is not fully encompassed by the prescribed isodose. This does not necessarily mean that the scheduled plan would have been clinically inferior if the prostate volume had been closer to that on the planning CT; however, this artifact artificially amplifies the apparent difference between scheduled and adapted plans.
2. Conversely, the scheduled plan (on either the pCT or CBCT) appears to offer better bladder and rectum sparing, particularly for high-dose metrics, due to the smaller target volume.

For the opposite case ($V_{CBCT} < 0.85V_{pCT}$), the main artifact was worse OAR sparing in the scheduled plan, again as a direct consequence of relatively larger target volumes (see columns "$V < 0.85V_{pCT}$" in Table 2 ; Supplementary Figure S2 in the Supplementary Material).

Importantly, adaptation maintained high rates of goal satisfaction across all three prostate-volume rangesfor nearly every metric (see Table 2). In contrast, the quality of the scheduled plan depended strongly on the relative change in prostate contour volume between pCT and CBCT. For example, for the bigger prostate on CBCT, the scheduled plan showed extremely low percentage of sessions with satisfied goals, going down to only 2.3% for the SIB1 goals.

Combining all prostate volume ranges into a single analysis would obscure true effects due to opposing OAR trends: the adapted plan appears superior when $V_{CBCT} < 0.85V_{pCT}$ but inferior when $V_{CBCT} > 1.15V_{pCT}$. For target metrics, however, the adapted plan consistently outperformed the scheduled one, with prostate volume deviations affecting only the magnitude, not the direction, of the benefit.

Thus, we applied this exclusion criterion to ensure that only genuine anatomical changes between pCT and CBCT were captured, avoiding distortions caused by contour volume discrepancies. We emphasize that consistent contouring is essential for a fair and unbiased assessment of the benefit of oART. Importantly, these inconsistencies influence only the comparison between scheduled and adapted plans and do not compromise actual treatment quality, provided that CBCT contours are anatomically accurate.

We showed that even for the homogenized dataset, the adapted plan yielded statistically significant and markedly superior target coverage compared to the scheduled plan. OAR sparing, in terms of median values for the dose metrics, was comparable between the scheduled and the adapted plans, although some OAR metrics exhibited statistically significant differences. This outcome is expected given the prioritization schema in our treatment planning system: target V95% metrics along with SIB2 Dmax and Dmean are assigned the highest priority (Priority 1), whereas most OAR metrics are designated as Priority 2 (except Bowel and PRW Dmax, which are also Priority 1). We consider the observed statistically significant differences in OAR metrics to be clinically irrelevant. However, the percentage of fractions meeting the optimal constraints increased notably for bladder and PRW metrics with adaptation.

Our findings are in line with those reported in (6), where the authors analyzed prostate cancer patients treated with stereotactic body RT on a Varian Ethos system. They observed significant improvement for the target metrics, however, the results for OARs were more variable: while the maximum dose to the rectum (represented by D0.03ccm) decreased, it increased for the bladder, and remained unchanged for the sigmoid and bowel. Similarly consistent improvement for the targets but inconsistent effects on OAR have been reported in (7). In their retrospective analysis of 198 fractions from prostate bed patients treated on the Varian Ethos system, a reduction in the IQR was observed for all metrics, which aligns with our results. Smaller IQR indicates high repeatability of dose delivery with the adapted plan.

Comparable outcomes—substantial improvements for targets with limited or variable benefits for OARs—have also been reported for oART in vulvar (10), rectal (11), and pancreatic cancer (25). However, it was shown for 8 patients with pancreatic cancer that adaptation can be statistically significantly beneficial not only for the target but also for most OARs—if the OARs are prioritized over target coverage (26), or at least have the same priority level (27).

In (28) the benefits of adaptation were shown for 3 patients with gastric mucosa-associated lymphoid tissue lymphoma: the adapted plan showed better target coverage and decreased mean dose to liver and kidneys. Thus, both the target and the OARs benefited from the adaptation.

Moreover, even excluding the fractions with high difference in prostate volume relative to the pCT (which can cause among other effects also an artificial underdosage for targets with scheduled plans), we observed occasional instances of low dose coverage for PTV and SIB1 with scheduled plans ($D95\% < 80\%$). This finding further underscores the importance of oART. The results align with results from (6), where a low PTV coverage sporadically occurred, despite the rigid registration of the CTVs to the CBCT, which ensured consistent CTV volumes between the pCT and each CBCT.

Plan quality in terms of homogeneity and conformality was significantly better for the adapted plan. However, the difference between the adapted and the scheduled plans was not so drastic as reported in (29), where 15 patients with bladder cancer were retrospectively analyzed. The difference between our results though could be explained by the field geometry. In our clinic, an IMRT with a fixed number of fields (mostly 9 or 12) is preferred, while in (29) 3 arc VMAT was utilized. On the other hand, in (30) IMRT was used, and CN values were comparable with those reported in (29). However, both (29) and (30) analyzed bladder cancer patients in contrast to our study with prostate patients.

It is important to note that the comparison of adapted vs. scheduled plans should not be directly interpreted as a comparison between oART and conventional non-adaptive RT. In conventional RT, larger CTV-to-PTV margins are typically employed to maintain target coverage at the cost of OAR sparing: in (8), the authors compared the scheduled plan with larger margins against the adapted plan with reduced margins for postoperative prostate patients. They indeed showed that the tighter margins with adaptation still could provide at least as good coverage as conventional IGRT, furthermore, they led to significantly better OAR sparing. Another study (9) proved the benefits of oART with smaller margins (in comparison to IGRT with conventional margins) for prostate cancer patients for both targets and health tissues (presented by the dose to the body). Similar observations were made for bladder cancer (30) and gynecological cancers (31, 32).

We acknowledge that comparing adapted and scheduled plans on the anatomy of the daily CBCT does not fully reflect the true dosimetric advantages of adaptation, as additional anatomical changes (e.g., bladder filling or bowel gas motion) may occur during the adaptation process and influence the target coverage and OARs sparing (9, 10). In the Ethos system, it is possible to acquire a verification CBCT after adaptation but before treatment delivery. A more realistic dosimetric assessment would require contouring the targets and OARs on this verification CBCT and recalculating the dose-volume metrics. We have previously performed this analysis for 8 patients (19) and highlighted that the "delivered dose" provided by Ethos is of limited value, as it

relies on rigid contour propagation. Thus, this delivered dose, although quickly accessible, is not suitable for the realistic dosimetric comparison.

In this study, we demonstrate that even with reduced margins, optimal target coverage is achievable with oART, while still providing equal OAR sparing in comparison with non-adapted plans (with the same margins).

5. Conclusions

This study demonstrates that online adaptive radiotherapy provides substantial improvements in target coverage in a clinically realistic setting. Adapted plans consistently achieved better homogeneity and conformality meeting target coverage constraints in nearly all adapted fractions, while OAR sparing stayed the same and the observed differences were not clinically relevant. The reduction in interquartile ranges across dose metrics further highlights the robustness and reproducibility of oART. These findings confirm that oART enables high-quality, consistent treatment delivery and reinforces its value in routine clinical practice for prostate cancer.

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Data availability statement

The data analyzed in this study is subject to the following licenses/restrictions: Research data are stored in an institutional repository and will be shared upon request. Requests to access these datasets should be directed to hanna.malygina@uks.eu.

Ethics statement

The studies involving humans were approved by Ärztekammer des Saarlandes, Germany. The studies were conducted in accordance with the local legislation and institutional requirements. All patients gave written informed consent for retrospective, pseudonymized analysis of their data in the context of the PRAIRIE trial protocol (Ethics vote 111/23 by Ärztekammer des Saarlandes).

Author contributions

HM: Methodology, Formal Analysis, Visualization, Software, Data curation, Writing – original draft. BZ: Data curation, Writing – review & editing, Investigation. HA: Methodology, Writing – review & editing, Supervision, Investigation. MR: Writing – review & editing, Investigation, Methodology. YD: Conceptualization, Writing – review & editing, Methodology. MH: Project administration, Supervision, Conceptualization, Writing – review & editing. JP: Methodology, Conceptualization, Data curation, Writing – review & editing, Validation.

Conflict of interest

The Department of Radiation Oncology and Radiotherapy is a Reference Site for Siemens Healthineers Center of Excellence for Advanced Radiation Oncology. JP has received a speaker honorarium from Varian Medical Systems, Inc. MH has received a speaker honorarium from Varian Medical Systems, Inc. and is a member of its advisory board.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The author(s) declare that Generative AI was used in the creation of this manuscript. During the preparation of this work, the authors used a large language model (ChatGPT, OpenAI, version GPT-4) to improve readability and grammar. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fonc.2025.1662671/full#supplementary-material

DataSheet1.pdf (531.6KB, pdf)

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Associated Data

This section collects any data citations, data availability statements, or supplementary materials included in this article.

Supplementary Materials

DataSheet1.pdf(531.6KB, pdf)

Data Availability Statement

The data analyzed in this study is subject to the following licenses/restrictions: Research data are stored in an institutional repository and will be shared upon request. Requests to access these datasets should be directed to hanna.malygina@uks.eu.

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Review

CT Urography Findings of Upper Urinary Tract Carcinoma and Its Mimickers: A Pictorial Review

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Abstract: Urothelial carcinoma (UC) is the fourth most frequent tumor in Western countries and upper tract urothelial carcinoma (UTUC), affecting pyelocaliceal cavities and ureter, accounts for 5–10% of all UCs. Computed tomography urography (CTU) is now considered the imaging modality of choice for diagnosis and staging of UTUC, guiding disease management. Although its specificity is very high, both benign and malignant diseases could mimic UTUCs and therefore have to be well-known to avoid misdiagnosis. We describe CTU findings of upper urinary tract carcinoma, features that influence disease management, and possible differential diagnosis.

Keywords: CT urography; urinary tract imaging; urinary tract tumor; urothelial carcinoma; upper tract urothelial carcinoma; benign urinary tract lesions; urinary tract inflammatory disease

1. Introduction

Urothelial carcinoma (UC) is the fourth most frequent malignancy in Western countries, with a peak incidence in elderly (70 to 90-year-olds) and a three-fold man prevalence. Upper tract urothelial carcinoma (UTUC) accounts for 5–10% of all UCs [1,2], with double the incidence of pyelocaliceal tumors compared to ureter location. UTUCs are often associated with concomitant or recurrent bladder cancer, while the contralateral urinary tract is implicated only in 2–6% of tumors. Many risk factors have been identified in the development of UCs, in particular tobacco smoking, some herb consumption, and aromatic amines occupational exposure [3].

Local symptoms of UTUCs, represented by flank pain or lumbar mass, are usually due to advanced disease, while systemic symptoms like fatigue, fever, and weight loss are related to metastatic progression. Hematuria, either microscopic or visible, is the most common and early symptom of UC, and requires prompt investigation. In patient with positive cytology but negative bladder cystoscopy, a UTUC is highly suspected, and so an upper tract evaluation is needed. Flexible ureteroscopy allows direct visualization of ureter, renal pelvis, and collecting system, with the possibility of direct biopsy or aspiration cytology, but it is considered quite invasive. Among imaging techniques, computed tomography urography (CTU) offers the highest accuracy in UTUC diagnosis, with a pooled sensitivity of 92% and a pooled specificity of 95% [3,4]. Other imaging modalities, like magnetic resonance urography (MRU) have been tested, but have been proven to be inferior. In particular, the direct comparison of MRU and CTU showed a sensibility of 82.8–86.2% and a specificity of 83.1–83.3% for MRU compared to 96.6% and 87–91.5% of CTU, respectively [5], so present guidelines indicate CTU as the imaging of choice in the work up of hematuria [3].

ATTACHMENT 12
Purpose of the Project

2. CTU Technique

CT Urography has to be tailored to clinical indication and could be performed with different protocols, including at least an excretory phase [6]. An unenhanced phase is used to detect stones, calcifications, hemorrhages, clots, and to measure the attenuation coefficients of the renal and urothelial masses [7–9]. A corticomedullary phase, occurring between 30 and 40 s after contrast medium administration, is used to evaluate suspected vascular abnormalities or arterial enhancement [9,10], while a nephrographic phase, acquired 90–110 s after contrast medium administration, improves detection and characterization of renal lesions [9,11]. The excretory phase, obtained 8–12 min after contrast agent administration, assesses the abnormalities of the urothelium with the distension and the opacification of the collecting systems, ureters and bladder [8–12]. However, the main limitation of a multiphasic protocols is the high radiation exposure, ranging from 25–35 mSv [6]. To reduce radiation dose, a split-bolus injection of contrast medium could be used, obtaining a single combined nephrographic-excretory phase, lowering the effective dose to 17.5 mSv [13]. To improve the distension and opacification of the collecting system, different ancillary maneuvers can be employed, the most common being intravenous saline hydration and low-dose furosemide injection (Figure 1) [6].

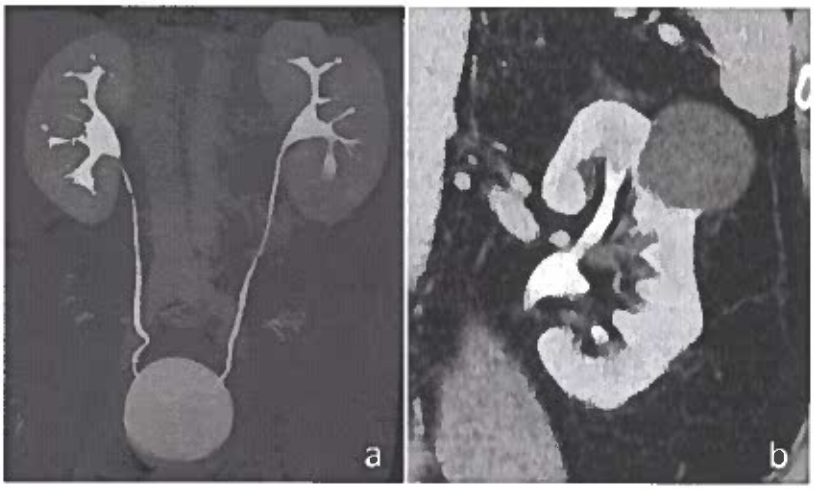

Figure 1. Computed tomography urography (CTU): MIP (maximum intensity projection) (**a**) and coronal (**b**) images. Furosemide administration allows distention of the entire urinary tract, without blooming artifacts due to high attenuation of intraluminal contrast medium; the split-bolus technique allows simultaneous luminal and parenchymal assessment.

3. Imaging Findings

Upper tract urothelial cell carcinomas appear on unenhanced phase as soft tissue masses, with lower density than renal calculi, except for indinavir ones [9,14–16]; intralesional and superficial calcifications can be seen and may appear granular, linear, or punctate [14,17–20]. After contrast medium administration, UTUCs show early enhancement, unlike non-enhancing clots, while in the excretory phase, they appear as filling defects or luminal narrowing in the urinary tract, best appreciated using a wide window setting, because small tumors may be concealed by the high attenuation of surrounding contrast medium (Figure 2) [9,14–16].

ATTACHMENT 12
Purpose of the Project

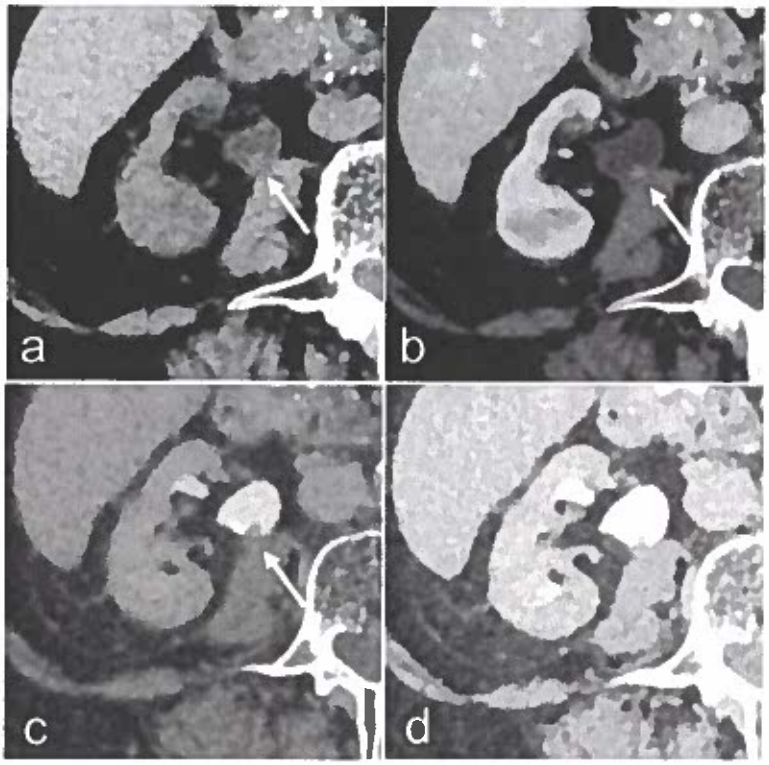

Figure 2. Small renal pelvis UTUC: a soft tissue lesion on unenhanced scan (arrow in (**a**)), shows homogeneous enhancement in the cortico-medullary phase (arrow in (**b**)) and appears as a filling defect in the nephrographic-excretory phase using a wide window setting (arrow in (**c**)). With wrong imaging settings, it results hardly recognizable (**d**).

Based on their morphology UTUCs may be differentiated in papillary tumors, flat lesions, and invasive carcinomas. Papillary tumors appear on CTU as single or multiple filling defects in the collecting system, varying from millimetric to broad basis wide tumors occupying the entire lumen [14,16,17]. When tumors involve the caliceal system, a calyx could be entirely missing in the excretory phase due to complete filling by solid tissue, the so-called "oncocalyx"(Figure 3a); calyx dilation and absence of urine opacification, classically described as "phantom calyx", occur if tumor develops in the infundibular neck determining its amputation (Figure 3b) [15,17,21,22]. When tumors involve the ureter, lumen occlusion is frequent and hydronephrosis can cause hypoperfusion of the renal parenchyma; on CTU, the solid ureteral mass is accompanied by a reduced nephrographic effect and a delayed contrast agent excretion (Figure 4) [16,17]. Flat lesions could manifest as a concentric or eccentric pyelocaliceal or ureteral wall thickening, not invariably causing luminal narrowing (Figure 5). Finally, UTUCs can present an infiltrative pattern with increased attenuation and stranding of periureteral and renal sinus fat (Figure 6). Direct involvement of renal parenchyma may be present in pyelocaliceal malignancy; on CTU, it is easily appreciated in the cortico-medullary phase thanks to early UC enhancement compared to renal medulla, while in the nephrographic phase, tumor tissue hypoenhancement is more difficult to differentiate from reduced nephrographic effect of the compressed adjacent parenchyma (Figure 7). Sometimes, in advanced cases, infiltration causes kidney enlargement, but with the preservation of the organ shape [9,16].

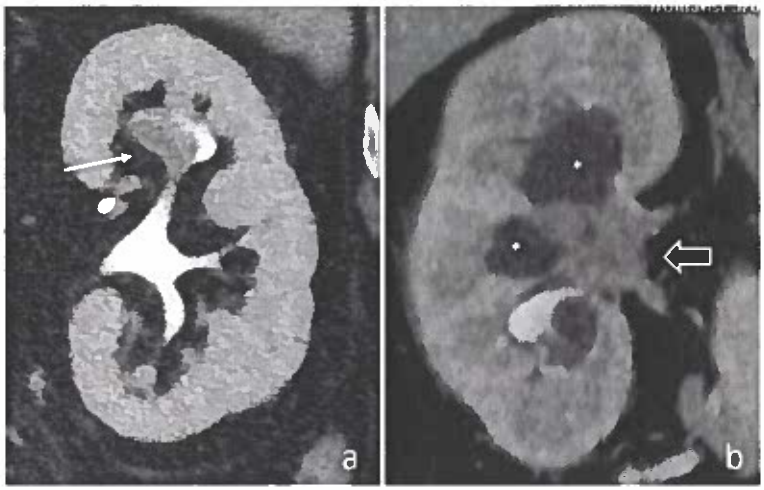

Figure 3. Pyelocaliceal papillary tumors: coronal nephrographic-excretory images (a,b). Solid tissue enlarges and obscures the superior calyx (arrow in (a)), the so-called oncocalyx. Solid pelvic-infundibular tissue (empty arrow in (b)) causes upstream non-opacified dilation (*), the so-called phantom calyx.

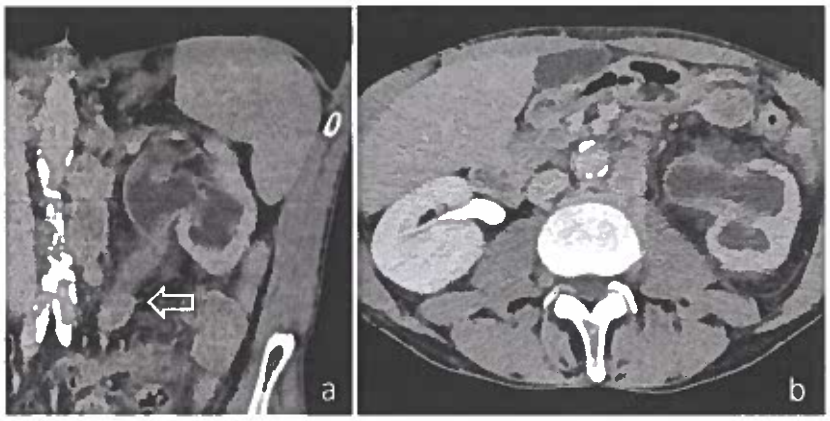

Figure 4. Ureteral papillary upper tract urothelial carcinoma (UTUC): nephrographic-excretory coronal (a) and axial (b) images. Solid tissue in the lumbar ureter (empty arrow in (a)) determines complete occlusion of the urinary tract with hydronephrosis. Note the reduced nephrographic effect and absent excretion of contrast medium in the left kidney.

CTU findings help distinguishing organ-confined diseases from advanced ones, but infiltrative tumors are correctly diagnosed only in 67% of cases; this low performance is due to microscopic invasion, not visible at imaging, or to misinterpretation of inflammatory changes as tumor involvement [23]. Therefore, in clinical practice multiple clinical, histological, and imaging parameters are used to stratify tumor risk and its consequent management. According to European Association of Urology guidelines, low-risk tumors, identified by unifocal disease, size < 2 cm, non-invasive aspect on CTU, and low-grade on cytologic or biopsy specimens, could be treated with kidney-sparing surgery (endoscopic ablation and segmental ureteral resection); on the other hand radical nephroureterectomy and systemic chemotherapy are indicated in case of multifocal disease, size > 2 cm, invasive aspect on

CTU, concomitant hydronephrosis, high-grade cytology, high grade or variant histology, or previous cystectomy [3].

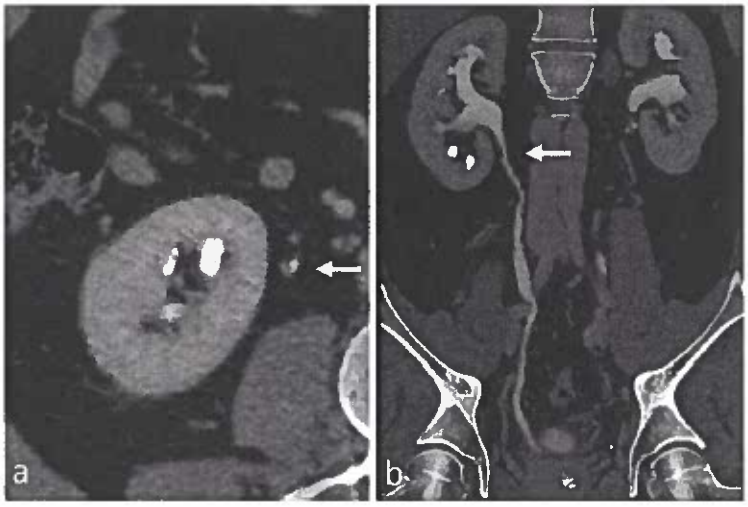

Figure 5. Flat ureteral UTUC: nephrographic-excretory axial (a) and CPR—curved planar reconstruction—coronal (b) images. An irregular wall thickening (arrows), without lumen narrowing, extends in the upper ureter. Urinary stones are visible in inferior calyces.

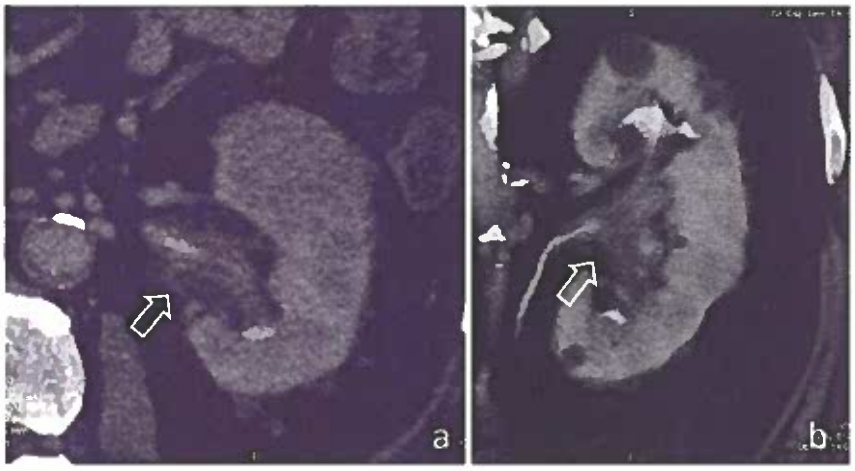

Figure 6. Pyelocaliceal infiltrative UTUC: nephrographic-excretory axial (a) and coronal (b) images. Extensive pyelocaliceal wall thickening with lumen narrowing causes diffused attenuation of the renal sinus fat due to tumoral infiltration (empty arrows).

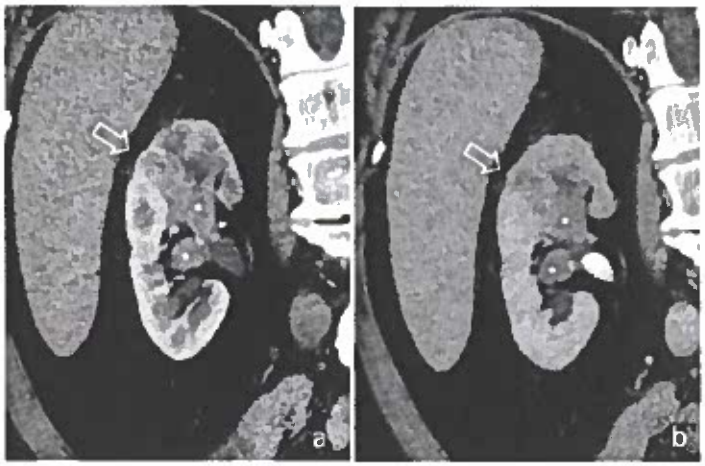

Figure 7. Caliceal infiltrative UTUC: coronal cortico-medullary (a) and nephrographic-excretory (b) images. Solid tissue occupies upper and medium calyces (*); the direct infiltration of kidney parenchyma appears hyper-enhancing compared to medulla in the cortico-medullary phase (arrow in (a)) and shows wash out in the nephrographic phase (arrow in (b)).

4. Mimickers of UTUC

Many pathological conditions may mimic CTU appearance of UTUC, both benign and malignant. Some CTU features could help differential diagnosis, but they are not always sufficient and so further diagnostic work-up may be required. Among these lesions, hypertrophied papilla, clots, suburothelial hemorrhage, renal papillary necrosis, symmetric wall thickening of the urinary tract due to inflammation or encasement, cystic pyeloureteritis, urogenital tuberculosis, and fibroepithelial polyp are benign lesions that should be considered to avoid an unjustified invasive intervention. On the other hand, renal cell carcinoma and renal lymphoma may be mistaken for UTUC and receive incorrect treatment.

4.1. Hypertrophied Papilla

Hypertrophied papilla, a benign anatomical abnormality, causes a pronounced concave impression on surrounding calyx that can mimic a filling defect in the excretory phase. The presence of a smooth contour with preservation of forniceal shape (Figure 8), along with the frequent presence of multiple similar aspects in the same kidney, allows correct diagnosis [24,25].

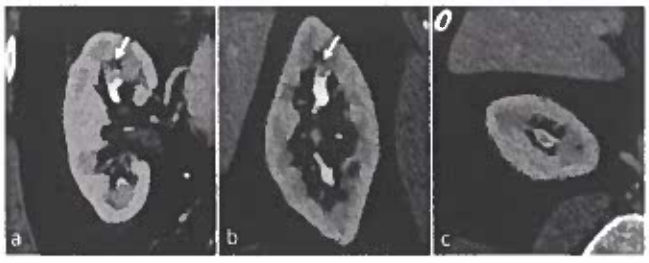

Figure 8. Hypertrophied papilla: nephrographic-excretory coronal (a), sagittal (b) and axial (c) images. A filling defect with smooth margins and regular shape is recognizable in the superior calyx (arrows); the forniceal structure is preserved.

4.2. *Blood Clots*

Blood clots are usually caused by trauma, neoplasm, renal lithiasis and anticoagulant therapy. They commonly manifest as slightly hyperdense lesions on unenhanced phase, without enhancement after contrast medium administration; in the excretory phase, they can be more easily differentiated from UTUC, because commonly entirely surrounded by opacified urine (Figure 9). In doubtful cases a further CT scan performed after changing patient position demonstrates a shift of the suspicious filling defect [7,9,12].

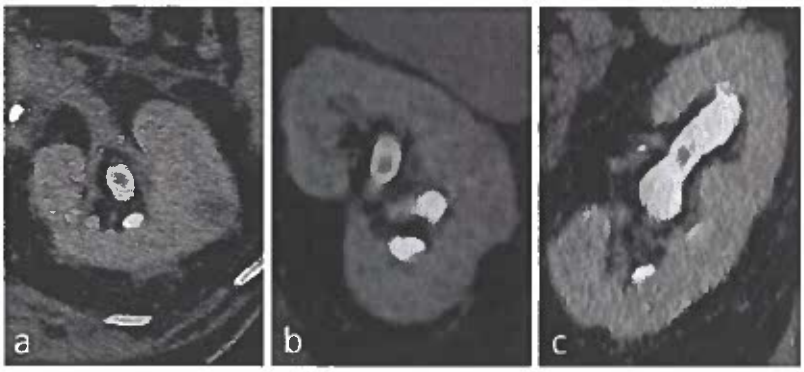

Figure 9. Blood clot: nephrographic-excretory axial (a), coronal (b) and sagittal (c) images. A small filling defect in the superior calyx without contact with the caliceal wall.

4.3. *Suburothelial Hemorrhage*

Suburothelial hemorrhage is a rare condition with diffuse renal sinus wall thickening due to intraparietal bleeding, presenting with flank pain and hematuria. This condition is related to bleeding diatheses such as anticoagulant treatment and hematological disorders. In the contrast enhanced and excretory phases, the renal pelvic wall shows diffuse soft tissue thickening with lumen narrowing, easily mistaken for a UTUC. The unenhanced phase allows the correct differential diagnosis demonstrating hyperdensity of the urinary tract wall due to hemorrhagic components (Figure 10) [26,27].

4.4. *Renal Papillary Necrosis*

Renal papillary necrosis (RPN), often presenting with hematuria, is due to an ischemic lesion involving the renal papilla; it is frequently associated with diabetes mellitus, sickle cell anemia, analgesic abuse and urinary tract infections [11]. RPN is recognizable only in the excretory phase, presenting as central erosion of the papilla filled with opacified urine, the teardrop-shaped cavity (Figure 11a) or the "ball-on-tee" sign (Figure 11b), or as erosion of the calyceal fornices filled with opacified urine, the "lobster-claw calyx". In the end stage, the sloughed necrotic papilla appears as a non-enhancing filling defect surrounded by contrast medium in the excavated calyx, the signet ring sing (Figure 11c) [14,25]. Beyond the possible presentation, RPN determines caliceal irregularity extending proximal to interpapillary line, with opacified urine located deep into the medulla, while calyceal irregularities due to UTUC extend toward renal pelvis [19].

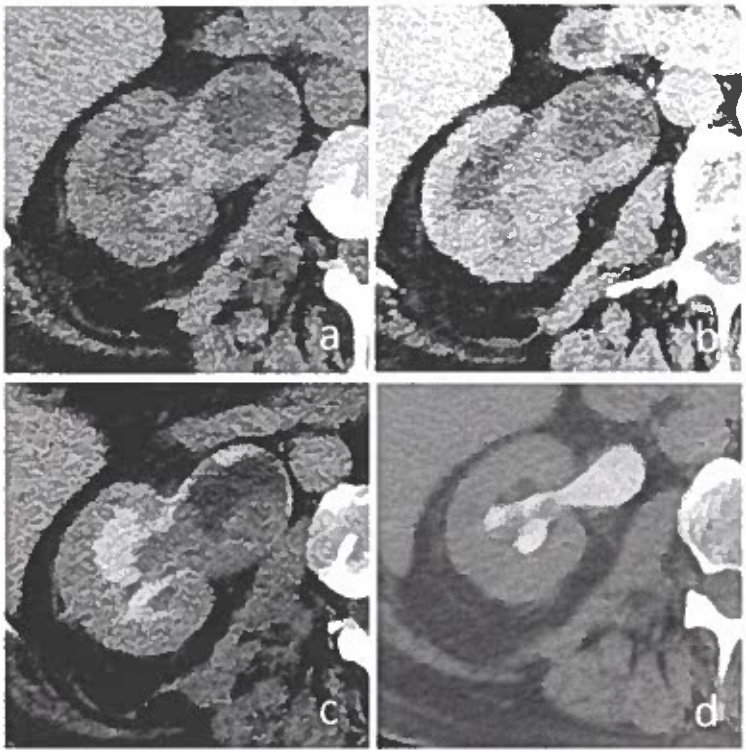

Figure 10. Suburothelial hemorrhage: axial images. In the unenhanced scan (a) diffuse hyperdense urothelial wall thickening is clearly visible. In the nephrographic (b) and excretory (c) phases wall thickening is hardly differentiable from a UTUC. Complete disease resolution on follow up CTU (d) confirmed the benign nature of previous extensive urothelial thickening.

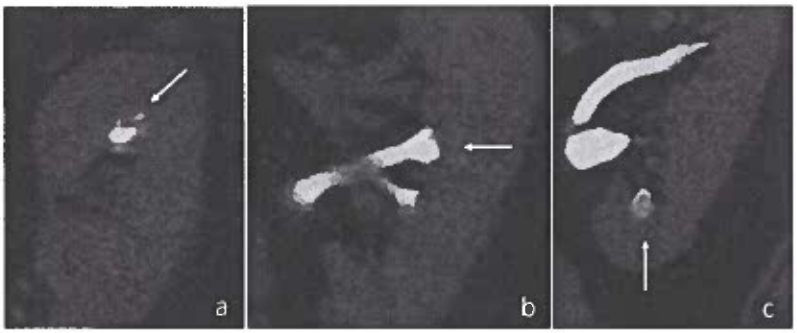

Figure 11. Renal papillary necrosis: excretory coronal images. The central erosion of a papilla appears as a focal spot of opacified urine inside renal medulla, with a teardrop shape (arrow in (a)) and a ball-on-tee shape (arrow in (b)); in the end stage necrotic papilla creates a filling defect in the excavated calyx, the signet ring sign (arrow in (c)).

4.5. *Inflammation*

Pyeloureteral wall thickening with increased attenuation of the surrounding fat is not a specific sign of UTUC but may be present also with urothelial inflammatory diseases. Differential diagnosis is not always possible on the basis of imaging alone, and so clinical, laboratory, and, sometimes, pathological findings have to be considered to decide proper management. The involvement of a longer part of the urinary tract is usually related to a benign disease, while UTUC is often associated with a shorter segment localization [7,12]. Other signs indicative of a benign disease are circumferential symmetric wall thickening, with diffuse urothelial enhancement, smooth margins, and symmetric and homogeneous attenuation of the surrounding fat (Figure 12); moreover, in doubtful cases, a follow-up CT may be useful to confirm benign nature of urothelial thickening (Figure 13) [28,29].

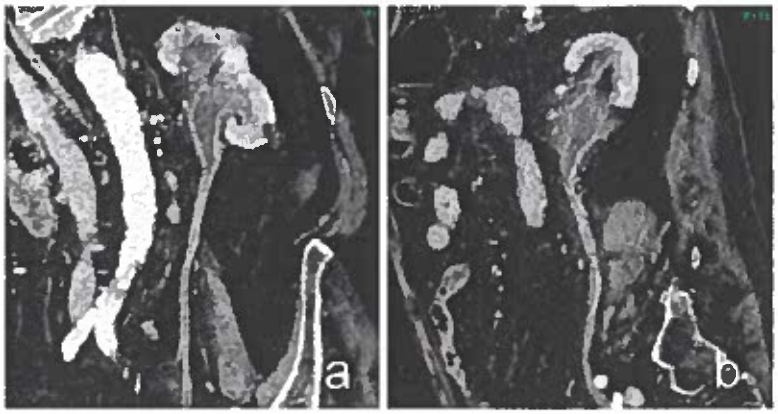

Figure 12. Inflammatory disease: CPR cortico-medullary images in corona (a) and sagittal (b) planes. Diffuse urothelial thickening with homogenous enhancement associated to haziness of sinus fat and mild hydronephrosis.

4.6. *Retroperitoneal Fibrosis*

Retroperitoneal fibrosis (RF) is a fibro-inflammatory disease characterized by the development of fibrotic tissue in the retroperitoneum; it could be idiopathic, associated to abdominal aortic aneurism, or secondary to other diseases. RF can cause ureteral encasement with obstruction and hydronephrosis. On CT it appears as enhancing solid tissue, generally isodense to muscle, that develops around the abdominal aorta, causing obscuration of fat planes, and medial displacement of the ureters (Figure 14) [29].

4.7. *Pyeloureteritis Cystica*

Pyeloureteritis cystica is a benign disease due to chronic inflammation of the urinary tract, characterized by multiple subepithelial cysts, arising from degeneration of von Brunn's nests. On unenhanced phase, the measurement of the attenuation coefficients of the cysts is usually not possible due to their tiny dimensions and, on excretory phase, they appear as multiple millimetric filling defects, often not detectable on nephrographic phase (Figure 15). The differential diagnosis between pyeloureteritis cystica and multifocal UTUC may be difficult. Nevertheless, the latter is usually characterized by presence of fewer and more inhomogeneous lesions [7,12,29,30].

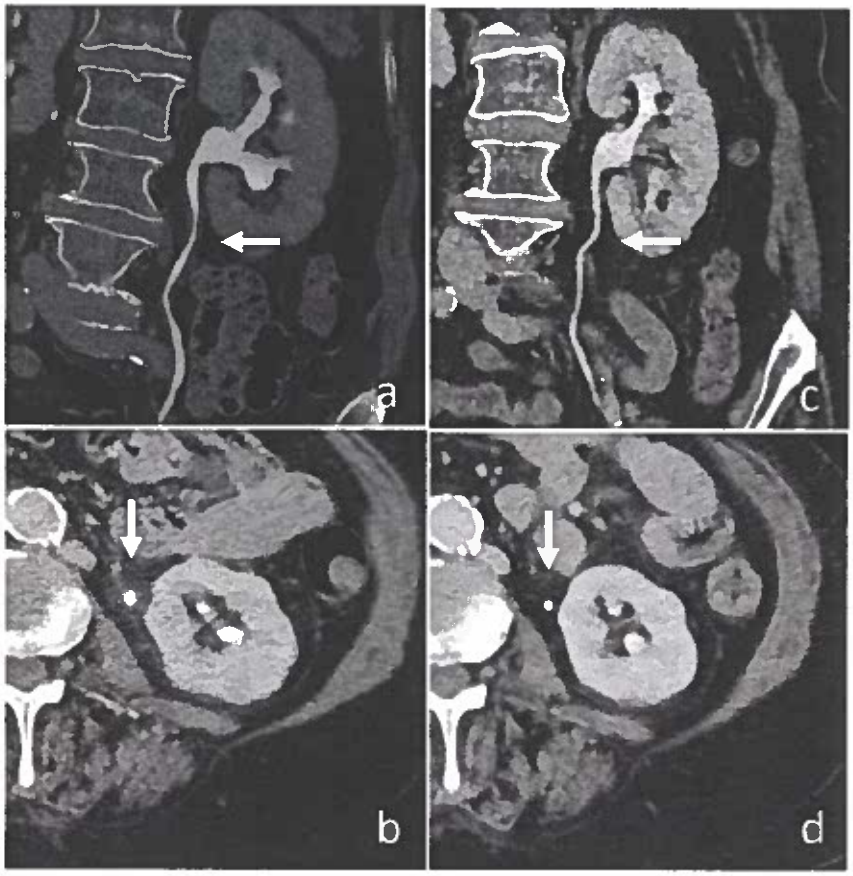

Figure 13. Inflammatory disease. Nephrographic-excretory CPR (a,c) and axial (b,d) images. A short ureteral wall thickening, with smooth margins and symmetric appearance, causes mild lumen stricture (arrows in (a,b)); clinical and laboratory data are indicative of an inflammatory disease. The follow up CTU performed 3 months later (c,d), demonstrates a complete resolution, confirming the benign nature.

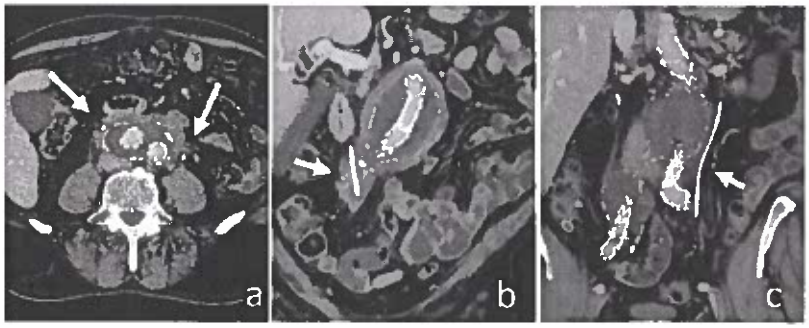

Figure 14. Retroperitoneal fibrosis. Nephrographic axial (a) and coronal (b,c) images. Low enhancing solid tissue surround an aneurismatic abdominal aorta, causing encasement and medial deviation with narrowing of both ureters (arrows), already treated with ureteral stents.

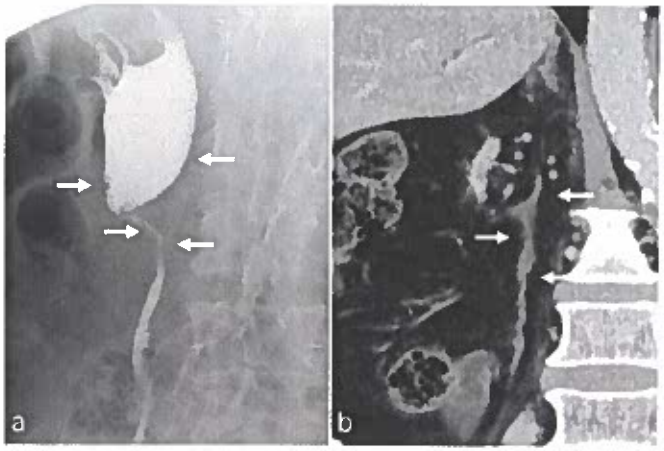

Figure 15. Pyeloureteritis cystica: ascending pyelography (a) and CT nephrographic coronal CT (b) images. Multiple small and regular filling defects are recognizable in the renal pelvis and proximal ureter (arrows in (a)), which correspond to tiny hypodense lesions inside a diffuse enhancing urothelial wall thickening (arrows in (b)).

4.8. Urogenital Tuberculosis

Urogenital tuberculosis (UGTB) accounts for almost one third of extrapulmonary TB cases, and 3% of patients with TB develop renal manifestations [31]. In the early stage of UGTB, the most typical imaging findings are papillitis, papillary necrosis and caliceal deformity, the so-called moth-eaten calyx [12,22,32]. During progression of the disease, granulomas coalesce and form the tuberculomas, i.e., caseous necrotic lesions with hypodense non-enhancing center, in direct communication with calyces [12]. At this stage, a fibrotic response develops, causing strictures with caliectasis, or amputation of the calyces, both characterized by a typical "rose-thorn" shape [12,22,31]. Moreover, pelvic stricture and retraction may be seen along with an irregular thickening of the pelvis and the ureter [22,33]. The differential diagnosis between UGTB and UTUC may be difficult. However, UGTB must be highly suspected when multiple different caliceal deformities coexist in the same patient (Figure 16) [28].

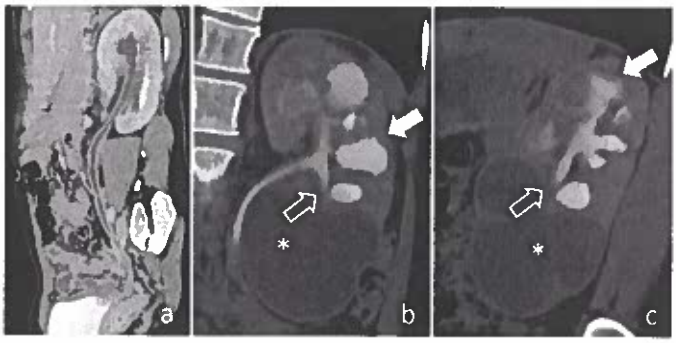

Figure 16. Urogenital tuberculosis: nephrographic-excretory CPR (a), coronal (b) and sagittal (c) images. Widespread enhancing urothelial wall thickening affects renal pelvis and the entire ureter (a). Multiple caliceal erosions with complete expulsion of necrotic papilla are recognizable in the upper and medium part of the kidney (full arrows), the inferior calyx presents a rose-thorn shape (empty arrows), while the lower pole is replaced by a large fluid cavity (*).

ATTACHMENT 12
Purpose of the Project

4.9. Fibroepithelial Polyp

A fibroepithelial polyp (FP) is a benign ureteral lesion, consisting of a fibrovascular stroma, covered by a layer of urothelium. It usually presents with hematuria or flank pain, and with a CTU aspect of a solid mass inside renal pelvis or ureter, so the differential diagnosis with a papillary UTUC is challenging (Figure 17). The correct diagnosis could be supposed only in the presence of the typical appearance of a long pedunculated mass with smooth margins, entirely surrounded by contrast medium in the excretory phase, except for the attachment site of the stalk [12,28,29].

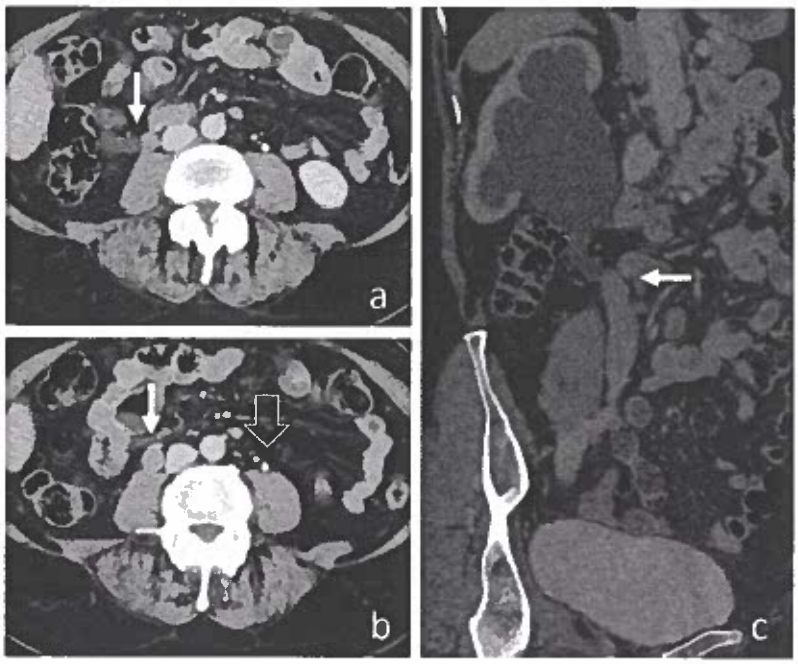

Figure 17. Fibroepithelial polyp: nephrographic-excretory axial (a,b) and CPR (c) images. A smooth-margin mass develops inside the ureter without associated wall thickening (arrows). Note complete lumen occlusion with upstream dilation and absent contrast excretion, by comparison with the contralateral normal ureter (empty arrow). When typical aspects are absent, differential diagnosis with UTUC is difficult.

4.10. Renal Cell Carcinoma

Renal Cell Carcinoma (RCC) typically appears as an expansive mass with well-defined margins and it is easily differentiated from urothelial carcinomas. Nevertheless, infiltrative RCCs could sometimes be difficult to distinguish from pyelocaliceal infiltrative UTUCs. Both malignancies show early contrast enhancement. However, the reniform shape is usually preserved in infiltrative tumors of the excretory tract, whereas a contour expansion can be seen in RCCs (Figure 18) [14,16,34].

4.11. Renal Lymphoma

Extranodal spread of lymphoma often involves the urinary tract, but primary renal lymphoma without systemic disease is quite rare. Lymphomatous tissue could develop from renal capsule or perinephric and hilar fat, determining a vascular encasement and renal sinus involvement. It presents as a homogeneous soft-tissue lesion on non-enhanced CT with poor enhancement after contrast

injection due to its hypovascularity, helping differential diagnosis with typical hypervascular RCCs and UTUCs. Lymphoma of the renal sinus could mimic the infiltrative pattern of UTUC, but lymphomatous tissue, due to its pliable nature, generally do not alter urinary tract shape nor causes hydronephrosis (Figure 19) [16,35,36].

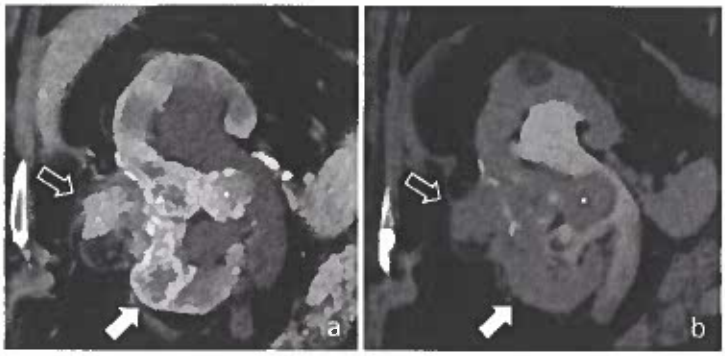

Figure 18. Recurrent RCC: cortico-medullary (a) and excretory (b) coronal images. A polilobulated lesion with inhomogeneous early contrast enhancement (full arrows) develops inside the renal parenchyma and extend in renal pelvis (*). The organ shape is altered and an exophytic mass is recognizable in the site of previous local surgery (empty arrows).

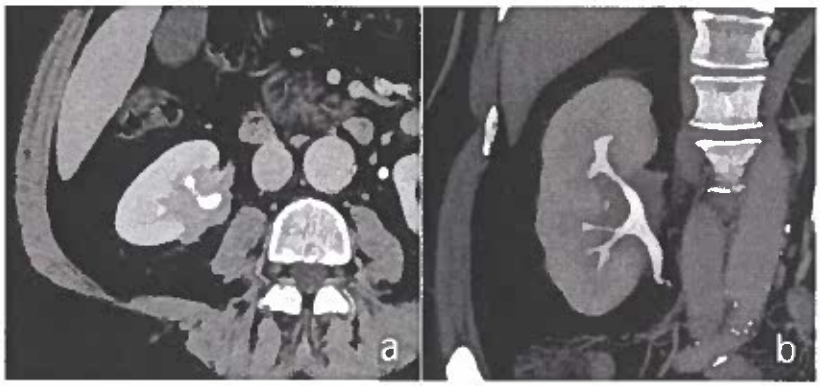

Figure 19. Renal sinus lymphoma: nephrographic-excretory axial (a) and MIP (b) images. Hypovascular and homogenous solid tissue diffusively involves renal sinus fat without distortion of pyelocaliceal system.

5. Conclusions

Computed tomography urography is a very useful tool in diagnostic workup of suspected upper urinary tract carcinoma. Some CTU features help to differentiate low-risk tumors from high-risk ones, leading to proper management. However, imaging findings could be nonspecific, and only the knowledge of possible UTUC mimickers guides a correct differential diagnosis, avoiding mistreatment.

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ATTACHMENT 12
Purpose of the Project

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

Abbreviations

CTU	Computed Tomography Urography;
FP	fibroepithelial polyp;
MIP	maximum intensity projection;
MPR	multiplanar reconstruction;
MRU	magnetic resonance urography;
RCC	renal cell carcinoma;
RF	retroperitoneal fibrosis;
RNP	renal papillary necrosis;
UC	urothelial carcinoma;
UGTB	urogenital tuberculosis;
UTUC	upper tract urothelial carcinoma

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ATTACHMENT 12
Purpose of the Project

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ATTACHMENT 12
Purpose of the Project

CARE DELIVERY/MODELS OF CARE

e13811

Publication Only

MRI-Linac radiation therapy outcomes in patients with prostate, breast and other advanced malignancies.

Lakhvir Kaur, Kim Mcmillin, Ashley Drokin, Amar J. Srivastava, Steven K. Seung, Matthew C. Solhjem, Stephen Blake Bader, Eric K. Hansen, Alice Wang Chesebro, Marka R. Crittenden, Kristina Hoot Young; Earle A. Chiles Research Institute at the Robert W. Franz Cancer Center, Portland, OR; Radiation Oncology Division, The Oregon Clinic, Portland, OR

Background: MR-guided radiation therapy offers an innovative approach, providing superior soft tissue contrast that enables clinicians to deliver higher doses to the target site with fewer fractions. The objective of the study is to assess objective response rates and adverse effects related to a community-based single-institution experience with the ViewRay MRIdian. **Methods:** An IRB-approved registrational trial was conducted at the Providence Cancer Institute starting May 2020, with data cutoff of September 2023. All patients treated underwent MR screening, and the target site(s) were treated using hypofractionated radiation therapy in ≤5 fractions. The primary endpoint was to assess adverse effects attributed to radiation therapy. Secondary measures included local recurrence-free survival (LRFS), distant metastasis-free survival (DMFS), overall survival (OS), and change in prostate-specific antigen (PSA) for patients treated definitively for prostate cancer. The assessments were performed under the guidance of experienced radiation oncologists. **Results:** From May 2020 to September 2023, n=257 patients received treatment on the MRIdian with a median follow-up of 430 days [range 4-1221 days]. One and 2-year LRFS was 92% and 87%, and excluding prostate and breast cancer, 83% and 70%. Definitive prostatestereotactic body radiation therapy(SBRT) was delivered to 117 patients and significantly reduced PSA (mean difference -6.27, $p<0.0001$), with no local failures to date. One and 2-year DMFS was 75% and 67%, though if excluding definitive prostate SBRT and partial breast irradiation, these were 48% and 33%. The OS rate at 1 and 2 years was 86% and 76%. Excluding prostate and breast cancer, the 1 and 2-year OS was 74% and 55%. Grade 3+ adverse events possibly or definitely attributable to radiation therapy were noted in 5% (n=13/257) of patients, including 2 possible treatment-associated deaths (bowel perforation following liver SBRT, and respiratory failure following lung SBRT and trastuzumab-deruxtecan systemic therapy). **Conclusions:** Our institutional experience with the MRIdian demonstrated high levels of local control, while overall survival was driven by out-of-field failures. Serious adverse events were infrequent, but more common in abdominal targets highlighting the need for careful planning and tight organs at risk (OAR) constraints, particularly if systemic therapy is delivered soon after radiation. Research Sponsor: None.

Prostate Cancer

RESOURCES > PUBLICATIONS >

What is Prostate Cancer?

Prostate cancer is one of the most common types of cancer even though prostate cancer only occurs in males. The prostate is a small walnut-shaped gland that produces the seminal fluid that nourishes and transports the sperm.

Many prostate cancers grow slowly and stay in the prostate gland, where the cancer might not cause serious harm; however, there are other types of prostate cancers that can be aggressive and can spread quickly.

When prostate cancer is detected early, an individual has the best chance for successful treatment.

Facts: According to the Illinois State Cancer Registry, there were 9,667 cases of prostate cancer diagnosed in Illinois in 2021. In 2021, 1,169 Illinoisans died from prostate cancer.

What are the Risk Factors of Prostate Cancer?

Factors that can increase the risk of prostate cancer include:

Older age

Prostate cancer is most common in males over the age of 50.

Race

Black people have a greater risk of prostate cancer compared to people of other races. In addition, Black people are more likely to have aggressive or advanced prostate cancer, but the causes are unknown.

Family history

Having a blood relative who has been diagnosed with prostate cancer, such as a parent, sibling, or child, may increase your risk of prostate cancer. Also, if you have a family history of the genes that increase the risk of breast cancer or a strong family history of breast cancer, you can be at a greater risk of prostate cancer.

Obesity

Obese or overweight people are more likely to have prostate cancer that is aggressive, and the cancer is more likely to return after the initial treatment.

What are the Symptoms of Prostate Cancer?

Prostate cancer may show no signs or symptoms in its early stages; however, in the later stages, prostate cancer can show symptoms such as:

- Trouble urinating
- Decreased force in the stream of urine
- Blood in the urine and/or semen
- Bone pain
- Losing weight without trying
- Erectile dysfunction

How is Prostate Cancer Diagnosed?

After prostate cancer screening, if the screening detects an abnormality, your doctor may recommend further tests to determine whether you have prostate cancer, such as:

Ultrasound

During a transrectal ultrasound, a small probe will be inserted into your rectum. Through sound waves from the probe, a picture of your prostate gland is created.

Magnetic resonance imaging (MRI)

In some cases, your doctor might recommend an MRI scan of the prostate to take a more detailed picture. Also, MRI images can help your doctor plan a procedure to remove prostate tissue samples.

Collecting a sample of prostate tissue

To determine if there are cancer cells in the prostate, your doctor may recommend a procedure to collect a sample of cells from your prostate (prostate biopsy). Prostate biopsy is often done using a thin needle that is inserted into the prostate to collect tissue. Afterward, the tissue sample is analyzed in a lab to determine if there are cancer cells present.

ATTACHMENT 12
Purpose of the Project

How to Prevent Prostate Cancer?

There is no sure way to prevent prostate cancer; however, there are things you can do to reduce your risk of prostate cancer including:

- Choose a low-fat diet
- Increase the amount of fruit and vegetables you eat each day
- Reduce the number of dairy products you eat each day
- Maintain a healthy weight
- Get regular exercise
- Stop smoking
- Drink less alcohol

Resources

American Cancer Society

CDC: Prostate Cancer

Mayo Clinic: Prostate Cancer

Prostate Cancer Foundation

Publications

Cancer Awareness in Illinois

2016 Prostate and Testicular Cancer Annual Report

Bladder Cancer

RESOURCES > PUBLICATIONS >

What is Bladder Cancer?

Bladder cancer is a common type of cancer that begins in the cells of the bladder, a hollow muscular organ in the lower abdomen that stores urine. The kidneys carry urine through the ureters to the bladder and out of the body through the urethra.

There are three types of bladder cancer

- Transitional cell carcinoma – cancer of the innermost tissue layer of the bladder. Most cancers of the bladder begin in the transitional cells.
- Squamous cell carcinoma – cancer of the thin, flat cells of the bladder. This type of cancer can develop after prolonged infection or irritation.
- Adenocarcinoma – cancer that begins in the glandular cells located in the lining of the bladder.

Bladder cancer can be described as:

- Superficial bladder cancer only affects the cells of the lining in the bladder
- Invasive bladder cancer spreads through the lining of the bladder to the muscle wall, nearby organs, and/or lymph nodes

According to the Illinois State Cancer Registry, in 2021, 3,147 new cases of bladder cancer were diagnosed in Illinois. Of these cases, 2,380 were in men and 767 in women. In 2021, 605 Illinoisans died of bladder cancer.

What are the Causes and Risks of Bladder Cancer?

The exact cause of bladder cancer is unknown; however, bladder cancer is often linked to exposure to certain chemicals and smoking. Bladder cancer occurs more often in men than women since men are most likely to smoke and work in the manufacturing industry. In addition, bladder cancer is more common in Whites than in any other race or ethnicity.

What are the Symptoms?

In the early stages, bladder cancer produces no signs or symptoms. One of the most common signs of bladder cancer is blood in the urine. Sometimes, the blood in the urine is not always noticeable. Some less common symptoms can include frequent urination, a feeling of urgency but not being able to go, and painful urination. If bladder cancer reaches a more advanced stage, symptoms can include bone pain, pelvic pain, unintended weight loss, and swelling of the legs.

How to Prevent Bladder Cancer

There is no definite way to prevent bladder cancer. However, you can reduce your risk by avoiding exposure to carcinogenic chemicals (people who work with hair dye, paint, metal, leather, and rubber are at increased risk), increasing your physical activity, drinking plenty of fluids, and not smoking.

Smoking damages every organ in the human body. More than 50% of bladder cancer cases are found in men who smoke and 20% in women who smoke. Eating a diet high in fried meats and fats and being overweight or obese also can contribute to bladder cancer.

Maintaining a healthy diet by consuming at least five daily servings of fruits and vegetables, particularly cruciferous vegetables like broccoli, cauliflower, and cabbage, may reduce the risk of developing cancer.

Resources

American Cancer Society

American Urological Association, Foundation, Inc.

Clinical Trials

National Cancer Institute

Publications

Cancer Awareness in Illinois

ATTACHMENT 12
Purpose of the Project

Malays J Pathol 2023; 45(3) : 333 – 352

REVIEW ARTICLE

Urolithiasis: History, epidemiology, aetiologic factors and management

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Abstract

Urolithiasis is defined as a disease diagnosed by the presence of one or more stones in the urinary tract. It is one of the oldest and most widespread diseases known to man, their discovery and characterisation chronology began with the civilisation's history. This pathology has a multifactorial aetiology, very frequent worldwide with geographic and racial variation, their prevalence is increasing in lockstep with socioeconomic development. In fact, this disorder affects between 2 and 20% of the population, with an approximate recurrence rate of 30% to 50% in 5 years. Furthermore, calcium-type stones, which are composed of calcium oxalate (CaOx) alone or a mixture of CaOx and calcium phosphate are the most common, accounting for more than 80% of cases. The medical management of urolithiasis is done by medical treatments and/or by surgical intervention for the stones extraction by the techniques such as extracorporeal shock wave lithotripsy (ESWL), ureteroscopy (URS), percutaneous nephrolithotomy (PCNL) and open surgery. However, various therapies, including thiazide diuretics and alkaline citrate, are used in an attempt to prevent stones recurrence induced by hypercalciuria and hyperoxaluria, but the scientific evidence for their effectiveness is less convincing. On the other hand, endoscopic and ESWL methods have revolutionised the treatment of urinary lithiasis, but these costly methods, can cause acute kidney injury and decreased renal function, in addition, do not prevent the probability of new stone formation. The deepening of our knowledge on all points relating to this disease is a priority for specialists in order to find adequate solutions for this disease. This review provides an overview of urolithiasis, its history, epidemiology, clinical manifestation, diagnosis and treatment methods.

Keywords: Aetiologic factors, diagnosis, epidemiology, history, management, urolithiasis.

BACKGROUND

Urolithiasis, also known as king's disease, is one of the most common diseases and a major public health problem concern around the world. The pathology is caused by an urinary biochemical imbalance between stone-forming inhibitors and promotors in a process called lithogenesis.[1] It is characterised by the presence of stones in the kidneys (parenchyma, calyx, etc.), or in the urinary tract (pelvis, ureter, bladder) (Fig. 1), therefore causing pain, bleeding and can lead to renal failure. The disease has been recognised since the dawn of history and methods of treatment have been reported in various medical writings from different civilisation. Treatment and prevention of urolithiasis recurrence requires a better understanding of the disease, the

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Malays J Pathol *December 2023*

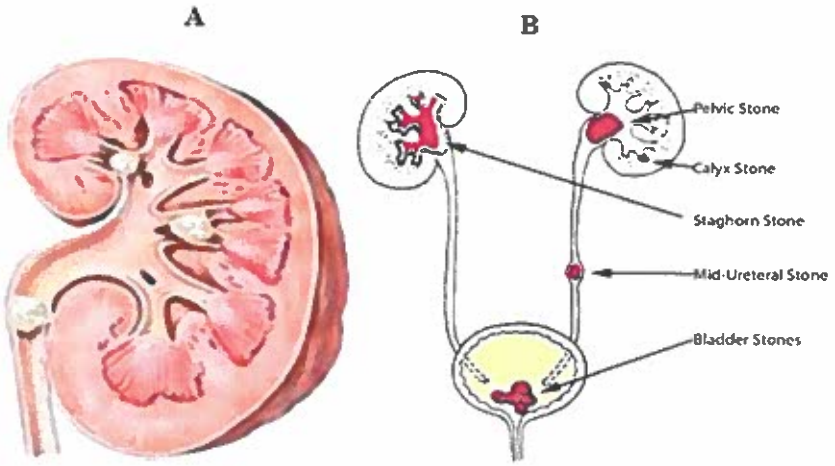

FIG. 1: Localisation of urinary stones in the kidney (A)[2] and in the urinary tract (B)[3].

mechanisms involved stones formation and the relationship that exists between other disorder.

Urinary Stones

The term "stones" is derived from the Latin calculus (pebbles)[4], and refers to a pathological biomineralisation product, defined as an agglomeration of crystals bound by an organic matrix. Except for rare types, which have a matrix content of approximately 65%, the latter accounts for 2 to 5% of the total mass of stones.[5] It is composed primarily of proteins, amino acid polymers, lipids and cellular compounds.[6–9]

The role and importance of this matrix has been explained in a paradoxical way by some researchers including Boyce (1968)[10], who proposed that it actively participates in the assembly of kidney stones, serves as a model and controls crystallisation within its limits.[11]

On the other hand, and in an opposite way, Vermeulen & Lyon (1968) considered that the matrix and its ubiquitous presence as a simple coincidence, because the stones crystallise in the urine with the presence a large macromolecules, and that proteins form a discontinuous layer around the small crystals whose sizes varies between 10 to 20 nm. However, they suggested that newly formed crystals with a macromolecular layer are less likely to dissolve during ionic and urinary pH changes, hence the matrix's importance in the formation of stones.[11,12] A third possibility has been proposed by Khan and Kok (2004), who suggest that the matrix compounds play different roles in two events, which do not necessarily take place at the same site. The first is manifested by the stone centre formation which involves the formation and retention of crystals and occurs in the short term. While the second involves their later constructions, it is a long-term event that occurs after the formation and maintenance of stones nest.[5]

History of the disease

The discovery and characterisation of stones chronology are not recent. It started and went in parallel with civilisation's history. Archaeological and paleontological documents clearly show that this pathology is one of the oldest human diseases. The earliest recorded urinary and bladder stones were identified by Shattock in 1905[13], found in Egyptian mummies and aged approximately 4400 BC. -JC for the first stone and from 4800 BC. -JC for the second.[13]

However, this disease has been cited in various scientific and literary writings throughout the human civilization's history (Fig. 2). The first literary references in relation to stone disease were revealed in of Asutu in Mesopotamia medical texts, between 3200 and 1200 BC. -JC. These writings describing symptoms and ordering treatments to dissolve stones such as the use of black saltpetre, ostrich eggshell, pine turpentine and the sex part of the donkey.[14–16] The old traditional Egyptian medicine has also reported therapeutic schemes for the treatment of urinary tract diseases, including stones which are

ATTACHMENT 12
Purpose of the Project

FIG. 2. Urolithiasis history.

found in the Ebers papyrus (1500 BC).[17,18] Also, the system of traditional Persian medicine dating back to 1000 BC describes the symptoms of stone disease and suggests methods of treatment based on the adoption of a bath and massage with scorpion oil, diet and the use mixture of some vegetables infusion.[14]

The Hindu writings of ancient India had mentioned this disease, mainly by two famous physicians Charaka and Sushruta (about 600 BC). The latter describes in their texts collection on the traditional medicine practice "*Sushruta Samhita*", the causes of stone formation. He recommended many medical treatments and provided a detailed description of the surgical procedure, including perineal lithotomy.[14,15,17,18] The contributions of the ancient Greeks and Romans are numerous and diverse. Hippocrates (460-377 BC) described kidney diseases and defined the symptoms of bladder stones. He also stated his warnings and concerns about the risks of performing lithotomy in their Oath "*I will not cut persons labouring under the stone but will leave this to be done by practitioners of this work*".[14,15,17,19,20] Ammonius of Alexandria (276 BC) was the first to suggest crushing stones in order to facilitate their removal. Cornelius Celsus (25 BC to 40 AD) described the abdominal pain of patients with urolithiasis, his description of perineal lithotomy marked a turning point in the history of urology. This technique was practiced with very little change and remained very useful until the end of the 18th century. Calus Plinus Secundus (AD 23–79), Galen (AD 131–200), and Paul d'Aegine (AD 625–690) were other notable physicians practising lithotomy.[14,15,17,21,22]

During the Arab-Muslim civilisation, stone extraction procedures were also known and frequently reported by Rhazes (865-925 AD), Ibn Sina (980-1037 AD) and especially by Abulcasis (Ibn Abbas Alzahrawi) (936-1013 AD), one of the fathers of modern surgery. The latter showed a considerable experience in surgery (the technique of perineal cystolithotomy), by modifying the lithotomy technique performed by Celsus and Paul d'Egina. His book "Al-Tasreef" clearly shows the improvement of this technique and the reduction of its risks. He appeared to be the first doctor to crush stones in the urethra.[14,15,17,23]

During the period from the Renaissance up to this point, there was a revolution and a rapid increase in intellectual creativity in many areas that are related to this disease:

- Sabuncuoğlu Serafettin (1385-1470) and Ahi Ahmed Celebi (1432-1522) had described a new technique of stones transurethral fragmentation and bladder irrigation, as well as rules to facilitate stones passage and dissolution.[15,24]
- Francisco de Romanis (1520) had made the first major scientific improvement since Celsus and Albucasis, to overcome the difficulty of locating the bladder neck.[14,15,25]
- Pierre Franco (1561), performed the first stone extraction by suprapubic lithotomy.[14,15,25]
- Jérôme Cardan (1501-1576), allowed the opening of the lumbar abscess.[14,15]
- Jacques de Beaulieu (1651-1714), introduction the "lateral lithotomy", this method was perfected and popularized.[14,15,17]
- William Cheselden (1722) and John Douglas (1719), extra-peritoneal approach.[14,15]
- Wollaston (1810), cystine, the first amino acid described, was isolated from urinary stones.[26]

- Jean Civiale (1824), introduction the modifications on the "primitive lithotrite" developed by Albucasis, to capture and fragment stones in the bladder.[14,15,17]
- Ingalls (1873), first nephrotomy.[14,15,25]
- Bigelow (1874), development of a stronger and harder lithotrite "litholopaxy", introduced into the bladder (with anaesthesia) to crush and remove stone fragments.[14,15]
- Max Nitze (1879), a lens system development for cystoscope.[26]
- Heinecke (1879), first pyelotomy.[14,15]
- Le Dentu (1881), first nephrolithotomy.[14,15]
- Max Brodel (1901), description of the kidney's avascular region.[14,15,25]
- Alexander von Lichtenberg (1906), radiological method for renal tract visualization.[26]
- Hugh Hampton Young (1904), cystoscopic lithotrite (1912) Rigid ureteroscopy.[14,26]
- Moses Swick (1929), intravenous urography.[26]
- Yutkin (1954), Electrohydraulic lithotripsy.[15,25]
- Goodwin (1955), the first percutaneous nephrostomy.[14,15,26]
- Marshall (1964), first experience of flexible ureteroscopy using a fiberscope.[15,26]
- Smith et Boyce (1967), introduction and popularisation of anatrophic nephrolithotomy for the treatment of staghorn stones.[15]
- (1970), percutaneous nephrolithotomy.[15]
- (1980), extracorporeal shock wave lithotripsy (ESWL).[14,15,25,26]

Epidemiology of urolithiasis

The epidemiological data of a given pathology can only be determined precisely if some factors such as geographical location, climate, race, sex, age, nutrition, and other environmental factors[27], endogenous and hereditary factors are taken into account.[28] However, according to Hesse *et al.* (2003), the "occurrence" parameter is determined by two factors: first, the incidence, which represents the number of the new disease cases per population, measured over a given time interval. The second is the prevalence, which is the proportion of sick people detected in a population at a given time.[27] Furthermore, the epidemiological characteristics and aetiological factors of urinary lithiasis are constantly evolving, reflecting to a large extent the health conditions, dietary habits and population's standard of living.[29]

The prevalence of the disease in industrialised countries has increased dramatically over the past 50 years. This transformation finds evidence in the economic progression which reflects changes in socioeconomic level, lifestyle modifications and changing eating habits. Globally, this disease affects approximately 2 to 20% of the population with variations between countries (Fig. 3).[27]

The United States being an outstanding example for studying changes in the epidemiological behaviour of the disease, due to the studies availability, high level of richness, large populations, as well as geographic and ethnic diversity. However, the study carried out by Boyce *et al.* (1956) between 1948 and 1952 (across all country states) estimated the average annual of hospitalists incidence at 9.47p 100,000, with a variation between States from 4.31 to 19.25 per 100,000.[30]

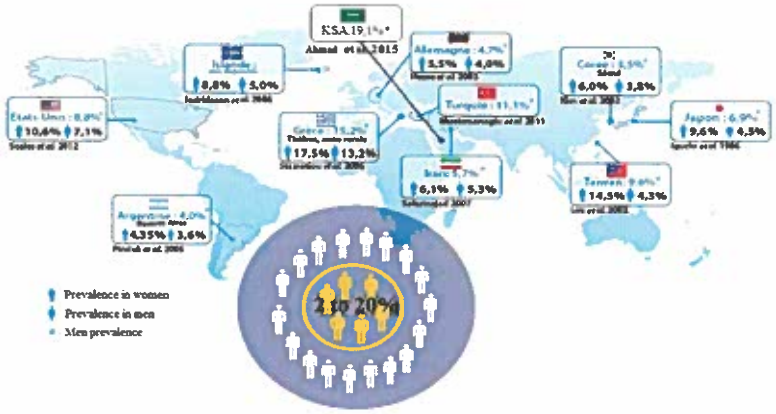

FIG. 3: Worldwide urolithiasis prevalence.

ATTACHMENT 12
Purpose of the Project

The work of Johnson *et al.* (1979) which lasted 25 years between 1950 and 1974 on the Rochester population, showed a significant increase of this disease in men, with an annual age-adjusted incidence around from 78.5 to 123.6 per 100,000 people. This parameter remained more or less stable in women with 36.0 per 100,000 people. The prevalence was also estimated in this population (Rochester) at 12% and 5% in men and women respectively[31], and another of 18.5% in Tennessee.[32] Later, Stamatelou *et al.* (2003) observed a nationwide increase in prevalence of 3.8 to 5.2% (from 1988 to 1994 and from 1976 to 1980) accompanied by variations in geography, ethnicity / race, age and gender.[33] Recent studies reveal the prevalence rate at 8.8%[34], and at 9.2%.[35] Forecasts for the 2030s estimated a prevalence at 9.5%.[36] Not far from USA, a similarity of epidemiological profile is marked in Canada compared to the last one, with a prevalence of 12%.[37,38]

In Europe, studies conducted after World War II showed a remarkable increase in the number of people affected by the disease (Table 1). The urolithiasis prevalence in the European Union was estimated between 5 to 10% in 2011, equivalent to 25 and 49 million people.[39,40]

In Germany, the disease trend was increased between 1979 and 2001, with an increase in the prevalence from 4.03 to 4.73% and the incidence from 0.54 to 1.47%.[27]

In Italy, the risk increased during these three decades and the prevalence tends towards 1.17% in 1983 against 1.72% in 1994[41], towards 4.14% in 2012 with an incidence of 2.32 / 1000P[42], regional variations were recorded with a major risk observed in Milano.[43] The picture is similar in Iceland with a prevalence of 4.7% in males and 3.2% in females.[44]

For Spain, UK and France, the disease frequencies are around 14.6% (2013-2014)[45], 7.14 to 11.62 % (between 2000 and 2010)[47] and 8.9% at age > 40 years (1994)[48,49] respectively.

The Eurasia zone is also marked by an increase in the incidence from 440.5 to 609.3 / 100,000P between 2002 and 2008 in Russia, from 53 to 6580 / 100,000P (1980 vs 2006) in Ukraine, 1030 and 2560/100,000P in Belarus (2004) and Tajikistan (2005) respectively[46].

In Asia, the work of Ogawa (2012) revealed an increase in prevalence in Japan from 4 to 10.8% between 1965 and 2005.[50] Zeng & He (2013) estimated the rate at 4% of China's urban population in 2008[54], and 9.6% in Taiwan between 1994 and 1996.[55] The Middle East had a higher rate of prevalence and major risk recorded in KSA with 19.1% between 2004 and 2008[57], Turkey with 11.1%[49] and Iran with 5.4%.[56]

However, the stones composition has changed considerably over these last decades, with a gradual increase in the frequency of calcium oxalate and calcium phosphate stones, even in the Eastern Hemisphere, where these stones were traditionally less common than uric acid and infection stones.[17]

Epidemiological studies carried out in different continents and countries indicate that calcium oxalate is very present with a levels varying between 51.3 and 78%, followed by calcium phosphate with a percentage varying between 11.9 and 13.8 %, then uric acid (from 6.9 to 11.9%), struvite (0.8 to 6%), cystine (0.6 to 2%), Brushite (1.1 to 1.5%) and finally the other components (0.1 to 1.1%).[28,29,39,50,60-62]

Urolithiasis recurrence is described as the disease reappearing in some patients after a period of time, which appears to be completely cured. It is a major issue for both patients and doctors. This parameter is a difficult subject to classify as a fundamental value, due to the heterogeneity of the factors involved, as well as the scarcity of studies that provide reliable data.[63] Generally, the recurrence rate is estimated at 30 to 50% within the first 5 years after the discovery of the first stone and from 50 to 60% within the next 10 years.[28,36,60,64]

In Morocco, a developing country, where access to healthcare is not the same across the country, which can lead to a loss of information about the disease. In addition, dietary habits differ from one region to another, and many patients rely on traditional medicine to initiate this disease, especially among the mountain population. In addition, there is a lack of studies regarding this disease, except for a few publications which have mainly focused on determining the stones composition collected in certain regions. From all the above, we could think that the epidemiological profile is far from reality and differs from one region to another.

However, the prevalence of urolithiasis in Morocco varies between 3.76 and 16.3% according to Joual *et al.* (1997).[65] The study conducted by Boumzaoued *et al.* (2015) in Moulay Ismail Military Hospital at Meknes reveals that the intra-hospital prevalence is 25.36%, with a male/ female ratio of 3.1, an average age of 47.1 years and the left side dominance compared to the right side (60.02 versus 35.84).[66] According to Laziri (2009),

ATTACHMENT 12
Purpose of the Project

Russia	2002 vs. 2008	440.5 vs 609.3/100,000			Absolute number of urolithiasis cases:	
Ex USSR					629 453 vs 704 373	
Moscow	1980-2008	17 vs 468.4			- Geographic variation	
Ukraine	1980-2006	53 vs.6580			- Urinary stone type (in St. Petersburg):	48
Kyrgyzstan	1980	48			Ox 66%	
Turkmenistan	1980	24			P 20.8%	
Uzbekistan	1980	30			AU/U 10.5%	
Belarus	2004	1030			Cys 2.7%	
Tajikistan	2005	2560				
Turkey	2468	1.7% (2008) M/F 1.4 vs 1.9	11.1% M/F 10.9 vs 11.2		- Ethnic variation - Recurrence rate: 16.7% after 1 year, 35.7% after 5 years.	49
					-CaOx (M/F) 35.1/17.9 →74.9/63.1	
					-CaP (M/F) 4.2/9.1 →6.5/12.8	
Japan	1965 vs. 2005	0.437/10000P vs. 1.43/10000P	4 vs 10.8% M/F 4.7/2.1% (1965) M/F 15.1/6.8% (2005)		-Mix (M/F) 44.4/44.3 →10.7/14.4	50
					- Infection stone (M/F) 7.5/23.3→14.5/1.1	
					-Urate (M/F) 4.6/1.4 →5.5/2.2	
Japan	1965 vs. 1995	68.9/100,000 vs 54.2/100,000 M/F 100.1/55.4 Vs M/F 81.3/29.5			- Risk of upper urinary tract stones occurring: M/F 4.3/1.8% (1965) Vs 9.0/3.8% (1995)	51
Korea	2009	8,298 inpatients 1,555 outpatients	457/100,000 M/F 589.09/326.64		-Incidence inpatients 133.0/100000 M/F 158.32/108.01 -Incidence outpatients 324.02/100000 M/F 430.78/218.64	52

ATTACHMENT 12
Purpose of the Project

China			1-5 and 2.0/100,000P	1 and 5 %	-Rate M/F 1/3 et 4/1 -67.7-89.6 % of patients aged between 21-50 years	33
China	2008	1169651 urban		4% M/F : 4.8/3.0%	- Prevalence in the north 4.1% vs 1.0% in the south	34
Taiwan	1994-1996	4588		9.6% M/F 14.5/4.3%	Geographic variation	35
Iran	2005	7649	1451/100,000	5.7% M/F 6.1/5.3	- Recurrence rate: 16% after 1 year, 32% after 5 years 53% after 10 years	36
KSA	2004-2008	5371 H 4871 F500		19.1%	-Ethnic origin variation -Higher prevalence among Egyptian (29.5%) and Pakistani (24.9%)	37
Brazil	1996vs. 2010			-Number of hospitalisations 0.36 vs 0.61% -M/F 49.9 vs 50.1%	- Number of hospitalisations ↑ 69% -5% higher during the December to March - Ethnic variation : 63.2% white 35.8% black 0.7% Asian 0.2% Indian.	38
Argentina (Buenos Aires)	2006	1086		3.96% M/F 4.35/3.62%	subjects over 19 years, the prevalence rate =5.14% with M/F 5.98/ 4.49%	39

CaOx : Calcium oxalate; AU : Uric acid; Mix : Mixture stone; CaP : Calcium phosphate; Cys : Cystine; ↑: Increase; M/F : Male/Female ratio; Ox: Oxalate; P: Phosphate; AUA: Uric acid/ Urate.

ATTACHMENT 12
Purpose of the Project

the average of annual hospital incidence rate is estimated at 30 per 100,000 in the Settat province.[67] In children, a prevalence of 0.83% was revealed between 2003 and 2013 in the Hassan II University Hospital Center in Fez.[68] The cumulative frequency was estimated at 0.25% during the period from 2000 to 2012 in the Meknes region, and an average hospital incidence rate was estimated at 21/100,000 in the paediatric surgery department of the Meknes regional hospital.[69] Regarding the stone composition, some researchers have found that calcium oxalate monohydrate is the major constituent, followed by uric acid, carbapatite and struvite.[67,70–72]

Clinical manifestation

Urolithiasis can remain asymptomatic for a long time, so it can be observed unexpectedly during an imaging examination or during a chronic kidney failure assessment.[73]

The initial presentation of urinary lithiasis is often accompanied by renal colic, which is pain caused by the displacement of a stone from the renal pelvis into the ureter, causes ureteral spasm and eventually obstruct.[62] The simple form of renal colic is frequent, characterised by sudden and intense pain, starting in the flank area radiating to the groin and progressing downwards and anteriorly into the genital area, as the stone descends into the ureter, with no peritoneal signs.[62,74,75] Generally, the pain is neither aggravated or reduced by a change of position, therefore may be accompanied by nausea and vomiting, adding also, that if the stone is lodged at the uretero-vesical junction, may cause a feeling of urinary frequency and urgency. However, all symptoms are relieved quite abruptly when the stone exits the ureter and passes into the bladder.[62] Other manifestations include persistent non-visible haematuria, intermittent visible haematuria, dysuria, penile oedema, enuresis, anorexia, and repetitive urinary tract infections.[63,75–78] The end-stage complications of infected stones can be life-threatening, including pyonephrosis, xanthogranulomatous pyelonephritis, perinephric abscesses and sepsis.[63]

Urolithiasis aetiologic factors

Determining and understanding the factors involved in promoting the formation of urinary stones are a very important part of treatment procedures. However, in order to implement a better treatment decision and have a satisfactory positive response, all the interactions and the complication of these factors must be taken into consideration.

1. Non-dietary risk factors

1.1 Family history

Urinary stones develop more frequently in people with a family history of the disease than in those without a family history. The risk ratio was estimated by Curhan *et al.* (1997) to be more than 2.57 times higher in individuals with a family history of the disease[79], and a recurrence threat of 1.2 was detected by Guerra *et al.* (2016).[80] The explanations about this factor remain limited on the likelihood of a genetic predisposition and environmental exposures combination shared by family members, mainly those related to eating habits.[63,64,81]

1.2 Relationship between urolithiasis and systemic disorders

Several diseases and systemic factors have been associated with an increased risk of urinary lithiasis occurrence. Primary hyperparathyroidism[82–84], renal tubular acidosis[85–87] and Crohn's disease[87–89] are affections that have been correlated with urolithiasis and increase the risk of stone formation.

A history of gout increases the risk of stone formation, both uric acid and calcium oxalate.[64] The Kramer & Curhan (2002) study, reported the chance to have a lithiasis history in people with gout at 49%.[90] These results were confirmed in men by a prospective study.[91] The relative risk (RR) of subsequent kidney stones in the age-adjusted (RR: 2.06) and multivariate (RR: 2.12) models was higher in patients with a confirmed gout diagnosis than in those without gout.[91]

Increased body size as assessed by weight and body mass index (BMI) is associated with an increased risk of stone formation, independent of other risk factors, including diet.[92] The magnitude of the increase in BMI risk is greater in women than in men.[92,93] The risk of stone formation in individuals with a BMI greater than or equal to 30 compared to those with a BMI of 21 to 23 was 30% higher in men, but almost twice as high in women.[64] Weight gain also increases the risk, weight gain of approximately 15.88 kg from early adulthood increases the risk of stone formation by 40% in men and by 80% in women.[64]

The study conducted by Taylor *et al.* (2005) revealed the positive association of diabetes with nephrolithiasis, independent of age, BMI, thiazide diuretic use and diet.[94] Daudon *et al.*

ATTACHMENT 12
Purpose of the Project

(2006) evaluated the types of stones in people with diabetes (type 2 diabetes), the proportion of uric acid stones was higher compared to calcium stones. The first type of stone was significantly 3 times higher in patients with stones with type 2 diabetes than in non-diabetic patients.[93] In the same lines, Cameron *et al.* (2006) demonstrate that a low pH level is the main risk factor for the uric acid stones formation.[94] In fact, diabetes may increase the risk of urinary stone formation by altering the urine composition. Insulin resistance is associated with high levels of free fatty acids in the plasma, which can enter the proximal tubular cells, interfering with the use of glutamine in ammonium production.[24] Likewise, this resistance contributes to the accumulation of ammonia and considerably reduces the pH, which favors the uric acid stones formation.[95] Low urine pH affects the ability of the urinary tract to excrete acid (citric acid), which increases the risk of stones containing calcium.[96]

The link between our pathology and hypertension has been adopted mainly in two opposing ways. The first considers that the incidence of urinary stones was significantly higher in hypertensive patients, i.e. people with high blood pressure are at an increased risk of developing a kidney stone.[97,98] On the contrary, the second shows that the risk of hypertension was higher in people with a history of nephrolithiasis and not vice versa. This association was independent of other risk factors recognised in these two pathologies.[99–101] In the same context, Gillen *et al.* (2005) established this hypothesis, but only in women.[102] In contrast, consumption of a DASH (Dietary Approaches to Stop Hypertension) type diet is associated with a marked decrease in the risk of urinary stone incidence.[103] Thus, it can reduce the risk of their formation by increasing the levels and volume of urinary citrate.[104]

The risk of cardiovascular disease has been associated with a history of urinary stone, although no causal relationship has been definitively established.[105] However, Ferraro *et al.* (2013) showed a modest increase in the risk of coronary heart disease in women with a history of stones, but not in men in prospective studies.[106] The survey by Alexander *et al.* (2014)and their prevalence is increasing. Kidney stone formers often have risk factors associated with atherosclerosis, but it is uncertain whether having a kidney stone is associated with higher risk of cardiovascular events. This study sought to assess the association between one or more kidney stones and the subsequent risk of cardiovascular events. Design, setting, participants, & measurements Cohort study of 3,195,452 people aged 18 years registered in the universal health care system in Alberta, Canada, between 1997 and 2009 (median follow-up of 11 years found a significantly higher risk of acute myocardial infarction of 40% in people with one or more episodes of stones. Concurrently, coronary angioplasty / coronary bypass surgery was 63% and stroke was 26%, with a greater effect in women than in men.[107] On the other hand, Domingos & Serra (2011) show that this relationship remained significant only for myocardial infarction in women with a risk of more than 57%[108], while the latter was 31% in the work of Rule *et al.* (2010).[109] In contrast, Fan *et al.* (2017) found that lithiasis disease was associated with a high prevalence of traditional and non-traditional risk factors for cardiovascular disease such as hypertension, albuminuria, chronic kidney disease, increased arterial stiffness and ankle brachial index, indicative of peripheral arterial disease.[110]

1.3 Environmental factors

Regions with higher average annual temperature and humidity appear to be contributing factors. People living under those conditions are prone to chronic dehydration, which results in low urine volumes and hypocitraturia, leading to an increased incidence of urinary stones especially of uric acid.[111,112] Seasonal variations have been mentioned with peak increases have been observed during the summer months.[113,114] Global warming trends are likely to shift and expand areas at increased risk for stone formation. A study modeling the impact of climate change on stone disease found that the fraction of the U.S. population living in areas at high risk for nephrolithiasis would increase from 40% in 2000 to 56% by 2050 and to 70% by 2095.[115]

1.4 Urinary risk factors

The crystallisation of stone forming salts is due to an abnormal urinary composition, of metabolic or environmental origin. These urinary risk factors are the basis for the diagnostic categorisation of stone-related diseases. Several factors can coexist in the same patient.[116] 24-hour urinalysis provides important prognostic information and direct treatment recommendations for the prevention of stone formation.

ATTACHMENT 12
Purpose of the Project

Hypercalciuria: Is defined as a calcium excretion in the urine, greater than or equal to 300 mg/day in men and 250 mg/day in women with a diet containing 1000 mg of calcium /day.[63,64,117] It affects approximately 20 to 60% of patients with stones[62,63,74,91,116] and contributes to calcium stone formation, by increasing the urinary calcium salt saturation and by deactivating negative charged urinary inhibitors.[116] The most common cause of hypercalciuria is increased absorption of calcium from the intestine. This disorder is also associated with low bone mineral density in the vertebrae, the causes of this latter are unknown.[116]

Hyperoxaluria: Where the oxalate urinary excretion is greater than 45 mg/day. This excretion can be present in 20 to 40% of patients affected by the disease, and the major risk is observed more in males than in females.[64,75,82] However, it should be noted that the risk of stone disease begins well below this oxalate excretion value. This may be due to the primary hyperoxaluria that causes the increased hepatic oxalate production or increased absorption in the short bowel syndrome called enteric hyperoxaluria (acquired), in which the intestine is overexposed to bile salts, resulting in increased permeability to oxalate. A diet low in oxalate and / or normal calcium to be raised, reduces oxalate urinary excretion.[63] In contrast, primary hyperoxaluria is rare and the result of autosomal recessive genetic disorders associated with oxalate synthesis. In fact, primary hyperoxaluria type I is caused by a mutation in the alanine: glyoxalate aminotransferase gene, while type II is caused by a mutation in the glyoxalate reductase / D-glycerate dehydrogenase gene.[62,116,118]

Hypocitraturia: Less than 320 mg/day urinary citrate excretion, found in 5-11% of new cases who developed stones. Citrate forms a soluble complex when it binds to calcium, thus preventing the binding of calcium to oxalate.[63,64] Hypocitraturia can be the result of distal renal tubular acidosis, chronic diarrheal syndrome, intestinal dysfunction, genetic factors, hypokalaemia, urinary tract infection, rich diet protein and low in alkali, but it is mainly of unknown aetiology.[116,117,119]

Hyperuricosuria: An elevated level of uric acid with excretion greater than 750 and 800 mg/day in women and men respectively, which results in spontaneous precipitation in solution. This precipitation can act as a scaffolding for crystalline aggregation of calcium oxalate and subsequent stone formation. Hyperuricosuria may be secondary to: uricosuric drugs, myeloproliferative disorders, primary gout or congenital disorders. Excessive intake of animal protein (especially purines) can increase uric acid excretion and decrease urine pH. The latter is a very important factor in controlling uric acid supersaturation.[63,117] However, allopurinol has been shown to be an effective agent in preventing the formation of calcium oxalate stones in patients with hyperuricosuria[120], also adding a decrease in protein intake is also useful.[62]

Cystinuria: Is a rare autosomal recessive disorder characterised by a reduced renal tubular reabsorption of the dibasic amino acids cystine, ornithine, lysine and arginine.[121] Over-excretion of cystine leads to stone formation due to their low solubility in urine at normal urine pH.[117] In fact, the solubility of cystine is pH-dependent (modest increase if the pH tends towards 7.5, greater increase if the pH exceeds 7.5) and varies according to the solubilises electrolytes and macromolecules. However, two genes responsible for cystinuria with multiples of mutations have been identified: the gene (SLC3A1) is responsible for type I cystinuria and completely recessive, while the gene (SLC7A9) is linked with non-type I (type II and III) and incompletely recessive. These two genes code respectively for two protein subunits rBAT and $b^{0,+}$ AT of a membrane transporter located in the renal proximal tube and epithelial cells of the gastrointestinal tract. Clinically, heterozygotes with type I mutations are silent, while heterozygotes non-I types (types II and III) have a wide range of urinary cystine levels and some even have symptomatic urolithiasis.[121-123]

Low urine volume: Is a common and modifiable risk factor, defined as a 24-hour urine volume less than 1L/ day, and present in 12 to 25% of lithiasic people. Low liquid consumption, with a low volume of urine production, produce high concentrations of solutes responsible for the stone formation in the urine. In addition, the risk decreases with high liquids intake, which stimulates the increase of total urine volume.[64,112]

Urine pH: A high urine pH leads to increased saturation of calcium phosphate, predisposing to develop lithiasis. A high urine pH can also lead to the formation of struvite stones, due to the low solubility of phosphate when excessive

ammonia is produced by the urea fragmentation. However, low urine pH predisposes to uric acid nephrolithiasis.[81]

Infection: Infection stones are formed when the upper urinary tract is infected by urease-producing bacteria, for example (*Proteus sp, Haemophilus sp, Ureaplasma urealyticum* and *Klebsiella sp*). These microorganisms hydrolyse urea to produce ammonia and hydroxide, increasing the urinary pH, consequently increasing phosphate dissociation to form trivalent phosphate. These latter bind to magnesium to form a "triple crystal" of struvite stone (magnesium phosphate ammonia) and / or calcium carbonate apatite. These stones mostly develop in a branched form (staghorn) which occupies a large part of the collection system.[116,117]

2. Dietary risk factors

Diet plays a very important role in influencing urine composition and therefore directly influences the risk of urolithiasis. The nutrients involved in this diet include calcium, animal protein, oxalate, sodium, sucrose, fructose, magnesium and potassium.[54,124,125]

Calcium: Excessive dietary calcium intake was considered to be a protective factor against urinary lithiasis formation, independent of other risk factors.[63] However, high dietary calcium intake binds with oxalate in the gut and subsequently reduces oxalate absorption.[125] Indeed, the study conducted by[126] reveals that the recurrence rate decreased by 50% in patients who followed a diet with a normal calcium intake (1200 mg/day) associated with a low intake of animal protein, compared to those who consumed a low calcium diet (400 mg/day). Unlike dietary calcium, calcium supplementation does not appear to reduce risk and may increase risk in older women.[125,127]

Oxalate: The proportion of dietary oxalate absorbed varies from 10% to 50% and is affected by concomitant dietary factors (such as calcium), intestinal flora and related diseases. In addition to this absorption, urinary oxalate is also derived from the endogenous metabolism of glycine, hydroxyproline, vitamin C and glycolate. However, the dietary contribution of urinary oxalate may be higher in stone formation. Up to one-third of patients with calcium oxalate nephrolithiasis may have increased dietary oxalate absorption, and in some cases, a deficiency in oxalate degradation by the bacteria *Oxalobacter formigenes* in the gut may be the cause.[63,64,81,128]

Potassium: An increase in dietary potassium intake has been considered to reduce risk in men and older women.[63] Potassium consumption potentially reduces calcium excretion in the urine and stimulates urinary citrate excretion.[17]

Sodium / sucrose: A high intake is directly proportional to urinary calcium and independent of calcium intake.[63] Salt consumption invariably increases calcium excretion, conversely, their reduction decreases calciuria especially in hypercalcious.[129]

Vitamin C (ascorbic acid): Can be metabolised to oxalate, higher intake may increase the risk of calcium oxalate stone formation.[87,64] According to Traxer *et al.* (2003), the consumption of 2 g of vitamin C per day increases urinary oxalate excretion by 20% in normal subjects and by 33% in lithiasis subjects.[130] The risk of stone formation was greater than 40% in men who consumed more than 1g of vitamin C, compared to men who ingested less than the recommended daily allowance.[131]

Vitamin B6: Is a cofactor in oxalate metabolism and its deficiency increases the production and excretion of oxalate in the urine. High doses of the supplemental vitamin B6 may be beneficial in some patients with primary hyperoxaluria type 1.[64] A high intake of vitamin B6 may reduce the risk of stone formation.[132,133]

Animal Protein: High levels of animal protein in the diet lead to high urinary oxalate, low pH, and low urinary citrate.[63] Red meat, canned fish, meat extracts and muscle are rich in purine, which increases the uric acid concentration and therefore promotes stone formation. By recommendation, protein intake should be limited to 1g/kg/day.[112]

Liquid intake: Low fluid intake (<1200 ml / day) predisposes to the stone formation. Increased water consumption results in urine dilution of constituents that may precipitate, as well as a reduction in the residence time of free crystalline particles in the urine.[127]

ATTACHMENT 12
Purpose of the Project

Urolithiasis diagnosis and management

1. Diagnostic
This is a very important step that gives a general idea of the nature and causes of the disease in order to choose suitable treatment methods. Different diagnostic tools are used to confirm lithiasis.

1.1 Initial investigation
Urinary tract stones diagnosis begins with a history focusing on key elements, include a family or previous history of urinary stone, duration and progression of symptoms, and signs or symptoms of sepsis. Physical examination is often more helpful in ruling out non-urologic disease.[134]

Metabolic investigations are important to predict the likely stone type (if the stone is not available for analysis), identify the secondary causes and metabolic risk factors, evaluate the prognosis, and guide the treatment. Typically, a metabolic workup including fasting blood and punctual urine samples, as well as 24-hour urine is requested.[135] Practically, we use the methods described below.

Urine test strip: allows to look for haematuria, nitrituria, leukocyturia, glycosuria, proteinuria, but also estimates density and pH.[136]

Cytobacteriological exam of urine (CBEU): performed to complete a positive urine dipstick, before initiating antibiotic therapy. It allows to recognise the non-glomerular character of a hematuria and to identify the germs especially the bacteria with ureasic activity.[73,136]

Blood culture: carried out systematically in case of fever over 38.5 °C. In the case of obstructive pyelonephritis, this examination looks for possible sepsis.[73]

Biological examinations: include creatinine, complete blood count (CBC), and blood ionogram.[73]

Crisatilluria: performed on fasting morning urine to determine the pH, density and pre-existing crystals in the urine.

1.2 Diagnostic imaging
In order to search the existence of an upper excretory tract dilatation or a stone, several methods are used, among which we cite:

Ultrasound: non-invasive, inexpensive, rapid, preferred for pregnant women and in patients with a renal failure stage.[74] It allows visualisation of the stone and more delicate for the visualisation of lumbar or iliac lithiasis. Its sensitivity is excellent for pyelocalicular stones and for those of the lower ureter (full bladder).[136]

Abdominal x-ray: easy to perform in emergencies, but it has a poor sensitivity for detecting the lithiasis with a poor specificity (Hamm *et al.*, 2001).[74] Therefore, this examination should not be done independently. However, the sensitivity is better when it is coupled with scanner.[74]

Intravenous Urogram (IVU): can show the entire upper urinary tract to the urethral opening, allows a fairly fine analysis, especially of the urothelium with a single iodine injection.[137] It has now replaced by the scanner without injection with almost unanimity. When the urologist wishes to visualise the urinary tree for an invasive procedure, this scanner is injected.[74]

Computed tomography (CT): an imaging method used to obtain cross-sections, reconstructed from measurements of the attenuation coefficients of the X-ray beam in the volume considered.[137] Injected or uninjected CT is the imaging test with the best sensitivity and specificity, giving dynamic 3D reconstructions. It helps to identify stones not visible on abdominal x-ray in particular uric stones, small stones, ureteral stones and to measure the density of these stones. It also allows to specify the differential diagnoses in nearly 50% of lumbar pain.[136]

1.3 Treatments

1.3.1 Dietary measures
Fluid intake is an essential component of treatment and should be adjusted to ensure that urine output is greater than 2.5 L/day. Balanced diet standardised in calcium (800 mg to 1 g/day), sodium (2 to 3 g/day), protein (0.8 to 1.4 g/kg/day), and limiting excessive intake of oxalate-rich foods to a threshold of 40 to 50 mg/day.[125]

1.3.2 Medical treatment
Renal colic treatment is based on the use of non-steroidal anti-inflammatory drugs (NSAIDs) which act by blocking the cyclo-oxygenases involved in the inflammatory cascade, reducing local edema and glomerular filtration rate.[74,137]

ATTACHMENT 12
Purpose of the Project

In recent years, the introduction of expulsion therapy based on drugs capable to facilitate the passage of distal ureteral stones. These are calcium channel blockers (such as Nifedipine) which act by relaxation of smooth muscle fibers and alpha blockers (such as Tamsulosin) that participate in peristalsis.[63,74,140] Yet despite their wide use, the evidence for the benefit of these agents in ureteral stones treatment remains weak.[63,141]

1.3.3 Surgical treatment

Surgical treatment aims to remove any stones in the urinary tract. Takes into account the stone location, its size, its composition, the urinary tract anatomy and the patient's morphology.

1.3.3.1 Extracorporeal Shock Wave Lithotripsy (ESWL)

Non-invasive method, applying waves created by an extracorporeal generator and focused on the stone in order to pulverise it. The stone localisation is done by ultrasound. The average success rate for the kidney is 60 to 80% and 80% for the ureter, depending on the stone's nature, their sizes and locations.[139,142]

1.3.3.2 Ureteroscopy (URS)

Invasive method that aims to remove stones stuck in the ureters or bladder, also can examine stones in the upper urinary tract. This procedure is painful and is performed by a ureteroscope in the form of a small wire that connects to a camera at the end. The latter is inserted into the urethra and passes into the bladder to remove stones.[143]

1.3.3.3 Percutaneous Nephrolithotomy (PCNL)

The procedure is invasive and consists in introducing a nephroscope through a percutaneous opening to fragment and extract stones larger than 2cm in diameter, or irregularly shaped (coralliform in particular).[75]

1.3.3.4 Open surgery

The use of open surgery for stone removal is declining due to the development of new non-invasive or semi-invasive methods such as ESWL, URS and PCNL. This method remains recommended for the treatment of large, coralliform stones where the predictable number of percutaneous accesses seems unreasonable.[144]

1.3.3.5 Alternative treatment based on medicinal and aromatic plants

Medical management of urolithiasis involves medical treatments and / or invasive surgical interventions to extract the stones, which may generate side effects and complications such as haemorrhage, hypertension, tubular necrosis, subsequent kidney fibrosis, renal failure, steinstrasse (several small stones blocking the ureter), pancreatitis, infection and persistent residue (potential nidus for new stone formation).[145–149] Research into treatment and prevention methods for this disease remains an avenue to be explored to avoid a possible recurrence in patients. In fact, the use of alternative methods, based on medicinal and aromatic plants (MAP) is very popular in the world, especially in developing countries. However, the exploitation of these traditional resources in research projects in order to verify experimentally the effectiveness of these resources and their applications is an issue and a challenge that must be addressed. Besides, ethnobotanical studies carried out in Morocco by various researchers have revealed the importance of some plants in the lithiasis treatment and in prevention of stones recurrence, as well as to relieve renal colic.[150–154]

On the other hand, in vitro studies show the effectiveness of plants extracts in inhibiting stone formation in different crystallisation stages (nucleation, growth, aggregation). Among these plants we can cite, *Rotula aquatica*[149], *Holarrhena antidysenterica*[147], *Origanum vulgare*[146], *Ammi visnaga*[155] *Phyllanthus niruri*[156], *Herniaria hirsuta*[157], *Trianthema monogyna*, *Macrotyloma uniflorum*[158], *Tamarix gallica* L.[159], *Punica granatum* L.[160], *Arbutus unedo* L.[161,162], act on calcium oxalate crystals. *Commiphora wightii*[163] *Citrus medica*, *Boerhaavia diffusa L.*, *Rotula aquatica*[164] inhibit struvite crystal growth. *Chenopodium album*[165], *Tribulus terrestris*, *Bergenia ligulata*[166] against brushite crystal growth. *Mentha pulegium* and *Eucalyptus camaldulensis* essential oils show a very important effect against the Bacteria with ureasic activity responsible on infection lithiasis formation.[167] In addition, in vitro studies on cell culture models as well as work on animal models have been carried out by deferent researchers and show the preventive effect of plants against cell damage and stone formation.[146,149,168–173]

ATTACHMENT 12
Purpose of the Project

CONCLUSION

This review work allowed us to take stock of urolithiasis disease, which has a multifactorial aetiology and is one of the major public health problems. The risk and frequency of this disease have increased steadily over the last decades, which at the same time has increased the care costs and created a burden on the health system. Despite the scientific and technological development which we are currently aware, the treatment methods used to relieve patients with urinary stones do not show the desired effectiveness, hence the need to find alternatives. Studies on the plants' active components are progressing, with interesting results that need to be confirmed at the clinical level. In addition, the prevention accompanied by a diet remains effective.

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List of abbreviations: *AU/U: Uric acid/ Urate rate; AU: Uric acid; BMI: Body Mass Index; CaOx: Calcium Oxalate; CaP: Calcium phosphate; CBC: complete blood count; CBEU: Cytobacteriological exam of urine; CT: Computed tomography; Cys: Cystine; DASH: Dietary Approaches to Stop Hypertension; ESWL: Extracorporeal Shock Wave Lithotripsy; IVU: Intravenous Urogram; M/F: Male/Female ratio; Mix: Mixture stone; Ox: Oxalate; P: Phosphate; PCNL: Percutaneous Nephrolithotomy; RR: Relative Risk; URS: Ureteroscopy; ↑: Increase*

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ATTACHMENT 12
Purpose of the Project

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ATTACHMENT 12
Purpose of the Project

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CT of the urinary tract revisited*

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ABSTRACT

Computed tomography (CT) of the abdomen is usually appropriate for the initial imaging of many urinary tract diseases, due to its wide availability, fast scanning and acquisition of thin slices and isotropic data, that allow the creation of multiplanar reformatted and three-dimensional reconstructed images of excellent anatomic details.

Non-enhanced CT remains the standard imaging modality for assessing renal colic. The technique allows the detection of nearly all types of urinary calculi and the estimation of stone burden. CT is the primary diagnostic tool for the characterization of an indeterminate renal mass, including both cystic and solid tumors. It is also the modality of choice for staging a primary renal tumor.

Urolithiasis and urinary tract malignancies represent the main urogenic causes of hematuria. CT urography (CTU) improves the visualization of both the upper and lower urinary tract and is recommended for the investigation of gross hematuria and microscopic hematuria, in patients with predisposing factors for urologic malignancies. CTU is highly accurate in the detection and staging of upper tract urothelial malignancies.

CT represents the most commonly used technique for the detection and staging of bladder carcinoma and the diagnostic efficacy of CT staging improves with more advanced disease. Nevertheless, it has limited accuracy in differentiating non-muscle invasive bladder carcinoma from muscle-invasive bladder carcinoma.

In this review, clinical indications and the optimal imaging technique for CT of the urinary tract is reviewed. The CT features of common urologic diseases, including ureterolithiasis, renal tumors and urothelial carcinomas are discussed.

1. Introduction

Computed tomography (CT) of the abdomen represents the standard of imaging for many urologic diseases. The main advantages of the technique include the wide availability, fast scanning, increased volume coverage in a single breath hold, high spatial and temporal resolution, lower susceptibility to variable patient factors and ability to assess different renal perfusion phases. The acquisition of thin slices and isotropic data allow the creation of multiplanar reformations (MPRs) and three-dimensional (3D) reconstructions in any desired plane without loss of anatomic details [1–5].

Non-enhanced CT (NECT) of the abdomen represents an accurate imaging modality for the investigation of renal colic or suspected urolithiasis. The technique is highly sensitive and specific in the diagnosis of

Abbreviations: CT, computed tomography; MPRs, multiplanar reformations; 3D, three-dimensional; NECT, non-enhanced CT; KUB, kidney-ureter-bladder; US, ultrasound; LDCT, low-dose CT; CECT, contrast-enhanced CT; RCC, renal cell carcinoma; CTU, CT urography; UTUC, upper tract urothelial carcinoma; MIBC, muscle-invasive bladder carcinoma; NMIBC, non-muscle invasive bladder carcinoma; HU, hounsfield unit; SWL, shock wave lithotripsy; PCNL, percutaneous nephrolithotomy; PN, partial nephrectomy; PF, perinephric fat; EP, excretory phase; BMI, Body Mass Index; ccRCC, clear cell renal cell carcinoma; pRCC, papillary renal cell carcinoma; chRCC, chromophobe renal cell carcinoma; fpAML, fat-poor angiomyolipoma; RO, renal oncocytoma; PEComa, perivascular epithelioid cell; NGP, nephrographic phase; IVC, inferior vena cava; CMP, corticomedullary phase; MRI, magnetic resonance imaging; ROI, region of interest; LN, lymph node; MIP, maximum intensity projection; TRUB, transurethral resection of the bladder; TNM, tumor-node-metastasis.

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ATTACHMENT 12
Purpose of the Project

Table 1
Suggested CT report template for preoperative assessment of suspected or proven renal cell carcinoma (PF: perinephric fat; IVC: inferior vena cava; AML: angiomyolipoma) [15].

Involved kidney

- **Nephrometry score:** Tumor radius (cm); Exophytic > or < 50 %, endophytic; Distance to the pelvicalyceal system (> 7 mm, 4-7 mm, < 4 mm); Location: Anterior/Posterior (A/P/X); Location regarding to the polar lines (above/below/cross/between); Extension into the renal vein
- **Extra-renal structures adjacent to the tumor:** Distance to the nearest anatomic structure, such as colon, small bowel, gall bladder, pancreas and renal hilar vessels
- **PF stranding:** (absent/present); Amount of PF: (scant/abundant)
- **Extension of tumor into PF, perirenal fascia or ipsilateral adrenal gland:** (absent/present)
- **Kidney location:** standard, high, low, ectopic
- **Kidney size (cm)**
- **Renal collecting system:** standard, duplicated
- **Vessels:** Distance of main renal artery origin to the first branch (cm) and to the renal hilum (cm); Accessory renal arteries; Length from IVC to right renal hilum (cm); Length from aortic edge to the left hilum (cm); Accessory renal veins
- **Parenchymal variant anatomy:** standard, dromendary hump, fetal lobulation, column of Bertin, renal cleft, congenital fusion/rotation
- **Benign pathology:** renal cysts, stones/calcifications, scars, AML

Contralateral kidney

- **Kidney size (cm)**
- **Enhancement:** normal, delayed
- **Pathology:** cysts, stones/calcifications, scars, AML

Others

- **Regional lymphadenopathy:** location, size, correlation with large vessels
- **Distant metastases**

urinary calculi, helping to predict spontaneous stone passage and/or to determine appropriate treatment planning [6–8]. However, due to the increased radiation burden, recommendations strongly advocate the use of kidney-ureter-bladder (KUB) radiography combined with ultrasound (US) as a primary imaging tool and the performance of low-dose CT (LDCT) in selected cases [6–8].

Contrast-enhanced CT (CECT) of the abdomen is the most commonly used diagnostic tool for the detection and characterization of renal tumors, including both cystic and solid renal masses [9–13]. CECT is also the modality of choice for staging renal cell carcinoma (RCC), providing valuable anatomic information to the surgeon [14,15].

CT urography (CTU) is a widely accepted tool for the routine work-up of macroscopic hematuria or microscopic hematuria, in patients with risk factors for urologic malignancies [16–22]. It represents the primary means of screening and staging the upper tract urothelial tumors (UTUTs) [16,20–22]. Choosing the appropriate technique is of paramount importance for the diagnosis of urothelial malignancies anywhere in the urinary tract [20–22].

CECT of the abdomen, including some form of CTU remains the standard for staging muscle-invasive bladder carcinomas (MIBCs). Regarding local staging, the technique is useful in diagnosing tumor invasion into the perivesical fat and/or adjacent organs, although it is unable to differentiate MIBC from non-muscle invasive bladder carcinoma (NMIBC) [23,24].

CT-based innovative approaches, including dual-energy, multi-energy, spectral CT and CT-based radiomics may improve the diagnostic performance of the technique in the assessment of urinary tract diseases [25–35].

In this review, we summarize data on when and how to perform a CT of the urinary tract. CT findings of common urologic pathologies, including ureterolithiasis, renal tumors and urothelial carcinomas are also presented.

2. CT of the abdomen: The urologists' perspective

Hematuria is a common symptom in urology and it is characterized as gross hematuria, when the blood is visible with naked eyes and microhematuria, when only detectable under the microscope. Common benign urogenic causes of hematuria include urolithiasis, infection and benign prostatic hypertrophy. Malignancies causing hematuria can originate from anywhere along the urinary tract [16–19,36].

The main predisposing factors for urologic malignancies include gross hematuria, male gender, age > 35 years, smoking, occupational exposure to chemicals, analgesic abuse, history of urologic disease, irritative voiding symptoms, history of pelvic irradiation, chronic urinary tract infection, exposure to known carcinogenic agents or chemotherapy and chronic indwelling foreign body [16–19].

All patients with gross hematuria should undergo a full urologic workup, as the etiology is malignant in up to 40 % of cases. Conversely, patients with microhematuria have a low risk of malignancy, ranging from 2.6 to 4 % [16–19]. CTU helps to elucidate the etiology of hematuria; and once a diagnosis is made, that assists the therapeutic planning and/or follow-up [16,20–21,36].

Urolithiasis usually presents with renal colic and is a common benign cause associated with hematuria. NECT of the abdomen can easily identify urinary stones [6–8]. It is important for clinicians not to miss clinically significant stones [37]. Although the stone size that is considered as "clinically significant" is debatable, stones smaller than 3-4 mm are mostly passed spontaneously and are not considered of clinical importance. Investigating the location of a stone is important, since it may influence treatment options. Endoscopic surgery is the treatment of choice for distal ureteral stones, thus differentiation of distal ureteral stones from phleboliths is important and often challenging, based on CT findings. Stone density, measured in Hounsfield Units (HU) is also essential for stone management. Stones with a mean CT density > 1000 HU are considered hard, making extracorporeal shock wave lithotripsy (SWL) an inappropriate option [38]. Stone density will also influence fragmentation efficacy, which will determine laser settings and predict operating times during intracorporeal lithotripsy. CT also plays an important role during percutaneous nephrolithotomy (PCNL) [8]. Anatomic information, regarding the exact stone location in the calyces, their relative position with the pleural space and the lower ribs, information regarding adjacent kidney structures, like colon, spleen and major vessels are important in order to achieve appropriate percutaneous access and avoid possible complications. CT-guided punctures may be an option in challenging cases, such as in patients with body deformities or in the presence of minimal hydronephrosis [39].

For urologists, hematuria is a presenting finding of a cancer, unless proven otherwise and RCCs invading the pelvicalyceal system or UTUCs are usually implicated. Large-sized tumors are hard to miss, but the same is not the case for small, usually endophytic or hypovascular renal masses and for small urothelial tumors, which require meticulous

ATTACHMENT 12
Purpose of the Project

Table 2
NECT findings of ureterolithiasis. [1]Stone size and location represent the most important predictors of spontaneous passage of a ureteral stone. [2]If CT secondary signs are detected and a stone is not seen, the possibility of a passed stone or obstruction due to other etiology, besides urolithiasis should be considered. [3]Ureteral dilatation rarely may not be seen in ureterolithiasis. [4]Hydronephrosis and perinephric fat stranding have 98% positive predictive value and 91% negative predictive value for the detection of ureterolithiasis (PF: perinephric fat; SWL: show wave lithotripsy).

	NECT findings	Remarks
Primary findings		
• **Stone burden**		crucial for management planning
	• number of stones	
	• stone size[1]: largest diameter, to the closest mm (use axial and coronal plane, bone windows settings and magnified views)	divided into stones measuring 5 mm, 5-10 mm, 10-20 mm and > 20 mm. Stones with a diameter of 5 mm have a 68% probability of spontaneous passage and stones with a diameter of 5-10 mm have a 47% probability of passage
• **Stone location**[1]	upper, middle or lower calyx; renal pelvis; upper, middle or distal ureter; urinary bladder	
• **Stone fragility**		may influence the outcome of SWL
	• heterogeneous stones: presence of internal hypodense areas	more susceptible to fragmentation
	• homogeneous stones: uniform internal structure (use thin sections, bone window settings)	less susceptible to fragmentation, more treatment sessions may be needed
• **Stone composition**		crucial for diagnostic and management planning; helps to predict the success of SWL
	• uric acid: 200-450 HU (< 500 HU)	great overlap in CT density of urinary stones, especially of small calculi
	• struvite: 600-900 HU	
	• cystine: 600-1100 HU	
	• calcium phosphate: 1200-1600 HU	
	• calcium oxalate monohydrate + brushite: 1700-2800 HU	
Associated findings		
• **soft-tissue rim sign**	• rim of soft-tissue attenuation around a ureteral calculus: corresponds to edematous ureteral wall	sensitivity, 77% and specificity, up to 92% for ureterolithiasis; more prominent for stones <4mm; seen in <10% of phleboliths
• **comet tail sign**	• eccentric, tapering soft-tissue area adjacent to a calcification	suggestive of phlebolith
• **radiolucent center**		suggestive of phlebolith
• **CT density**	• stone >> phlebolith	
Secondary findings[2] (signs of obstruction)		
• **ureteral dilatation**[3]		
• **hydronephrosis**[4]		
• **PF stranding**[4]	• increased attenuation of PF, thickening of perirenal septa and/or renal fascia	often not detected during the first 2 hours following the onset of acute flank; 8 hours may be needed to be optimally seen
• **perureteral stranding**	• increased attenuation of periureteral fat	
• **unilateral renal enlargement**	• may be more focal at renal poles (early phase)	may be seen in early or subtle obstruction
• **unilateral absence of hyperdense medullary pyramids**		
• **thickening of the lateroconal fascia**		
• **differences in renal parenchymal density**	hypodensity of the parenchyma of the obstructed kidney (due to edema)	
Findings useful in the planning of interventional procedures		
• **relationship of the kidney to surrounding organs**		
• **complex or variant renal anatomy**		
• **aberrant vasculature**		
• **selection of appropriate calix**		
• **distorted pelvicalyceal architecture or abnormal infundibular orientation**		
• **skin-to-stone distance**		helps in predicting stone-free-status after SWL
	• measured from the center of the stone to the skin surface (axial plane)	

evaluation with CTU. Obviously, flat urothelial lesions are challenging, but the radiologist should keep in mind that when wall thickening and contrast enhancement is reported on CTU, ureteroscopy under general anesthesia usually follows.

Histologic characterization of renal tumors, based on CT findings alone is practically unfeasible. Understandably this is a difficult task, since even a biopsy of a renal mass can be non-diagnostic in up to 8 % of cases [40]. CT plays a cardinal role in the characterization of renal cystic masses and staging of RCC [12–14]. RCC size, presence of tumor venous thrombus, regional metastatic lymphadenopathy, involvement of the adrenal gland and distant metastases are often included on a CT report. But surgeons would appreciate detailed imaging of the renal vessels, tumor's endophytic or exophytic nature and information regarding its vicinity to the renal hilum and the collecting system [15,41]. The RENAL nephrometry score is of great assistance, since it correlates with surgical decision making, surgical complications, postoperative functional outcomes, Cancer-Specific Survival and histologic factors such as tumor stage and grade (Table 1) [15]. Measuring the posterior and lateral perinephric thickness and assessing the extent of perinephric stranding may anticipate surgical difficulties in cases of partial nephrectomy (PN), which requires removal of the perinephric fat (PF) [42]. Equally important is the relative position of the kidney to the thoracic cage.

ATTACHMENT 12
Purpose of the Project

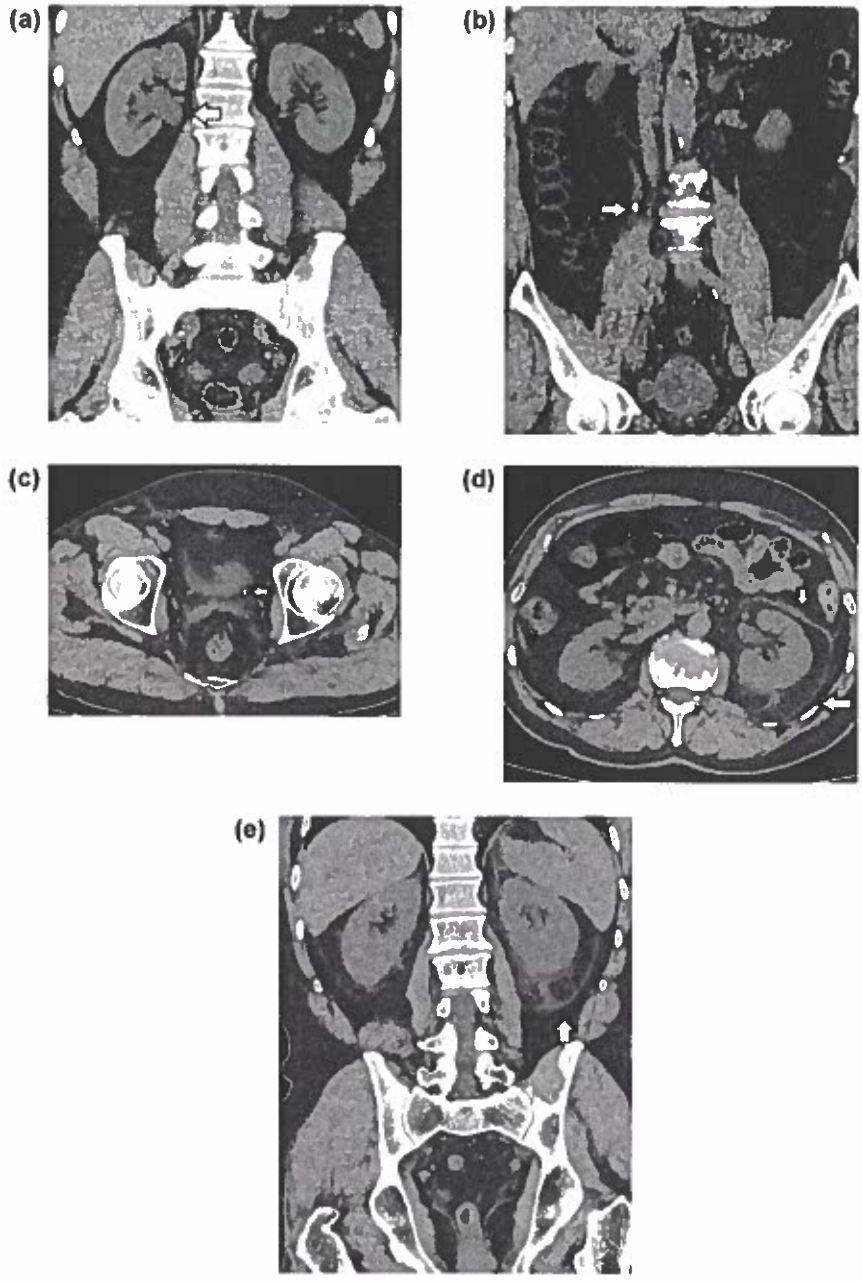

Fig. 1. Typical non-enhanced CT findings of ureterolithiasis in two patients. (a, b) Coronal reformations show a 4.5x6 mm stone (arrow, b) in the upper third of the right ureter, causing proximal ureteral dilatation and significant ipsilateral hydronephrosis (arrow, a) (c) Transverse image in the lower pelvis depicts a 2 mm stone (arrow) located in the left ureterovesical junction. (d) Axial and (e) coronal reformatted images in the same patient demonstrate secondary signs of ureterolithiasis, including thickening of the left renal fascia and perirenal septa (arrows), presence of fluid in the perirenal space and mild hydronephrosis

ATTACHMENT 12
Purpose of the Project

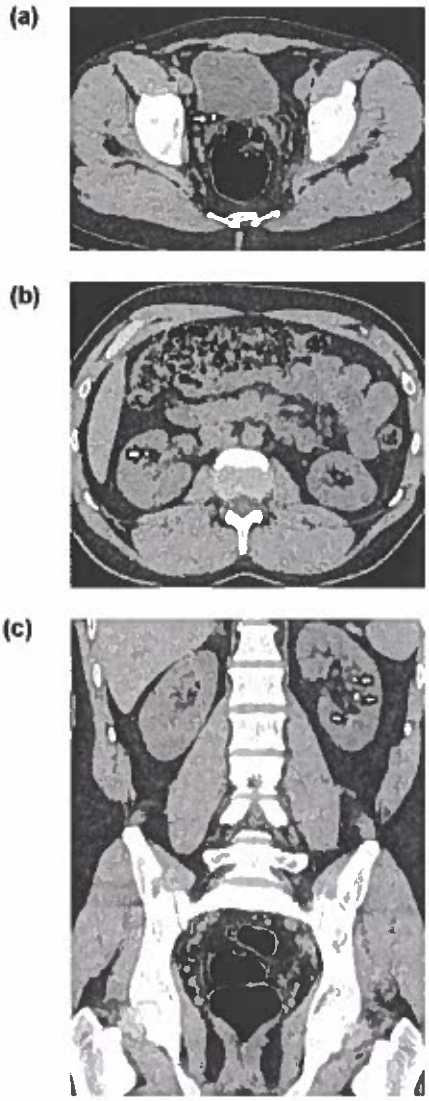

Fig. 2. Ureterolithiasis with absence of acute obstruction. (a) Axial non-enhanced CT image of the lower pelvis shows a 2.5x3.5 mm stone (arrow) in the right ureterovesical junction. The mean CT density of the calculus is 350 HU. (a) Axial and (b) coronal reformations depict absence of right hydronephrosis. Bilateral small renal calculi (arrows) are found to coexist.

Finally, when bladder cancer (BC) is suspected, it is always confirmed with conventional cystoscopy. CT provides mainly information regarding staging of advanced tumors and is of importance when the decision for radical cystectomy is made [23,24].

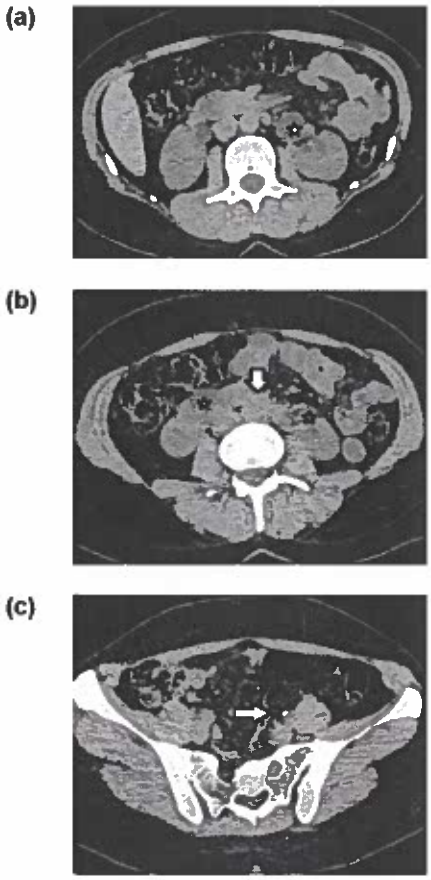

Fig. 3. Horseshoe kidney and ureterolithiasis. (a, b) Axial non-enhanced CT images show lower poles of the kidneys fused (arrow), in keeping with a horseshoe kidney. Bilateral hydronephrosis (stars) is also detected, marked on the left side. The cause is a 3x4 mm stone (arrow, c) located in the upper third of the left ureter. A thin halo of soft-tissue density is seen around the calculus (soft-tissue rim sign), a finding that is very specific for the diagnosis of ureterolithiasis.

3. Renal colic

Renal colic accounts for 1 % of the emergency department visits [6–8,43–47]. Approximately 14 % of men and 6 % of women will develop urinary tract stones during lifetime, with recurrence rates of 26 % within 5–10 years [8]. Since the first report by Smith et al., NECT of the abdomen has been established as an accurate technique for imaging renal colic or suspected urinary stone disease, with 95–98 % sensitivity and 96–100 % specificity for the diagnosis of urolithiasis [7,8].

NECT is performed rapidly, does not require bowel preparation or intravenous administration of contrast medium and has low interobserver variability. CT allows the detection of nearly all types of urinary stones, including those that are radiolucent on KUB radiography, such as

ATTACHMENT 12
Purpose of the Project

Table 3
Bosniak classification, version 2019 of renal cystic tumors, including CT findings, new definitions incorporated in the updated classification and recommendations for management (NECT: non-enhanced CT; CECT: contrast-enhanced CT) [12].

Category	CT findings	Definitions	Recommendations
I	well-defined, homogeneous simple fluid (-9 to 20 HU), smooth thin wall that may enhance, absence of septa or calcifications	• thin wall: < 2 mm	benign, simple renal cyst: no follow-up
II	well-defined, smooth thin wall a. cystic mass, few thin septa; septa and wall may enhance; calcifications of any type b. homogeneous hyperattenuating mass (> 70 HU) on NECT c. homogeneous nonenhancing mass < 20 HU at renal mass CT protocol; calcifications of any type d. homogeneous mass -9 to 20 HU on NECT e. homogeneous mass 21-30 HU on portal phase CECT f. homogeneous hypodense mass too small to characterize	• renal cystic mass: • < approximately 25 % of enhancing elements, based on subjective visual inspection • few septa: 1–3 • thin wall/septa: • (< 2 mm)	benign, simple renal cyst or highly likely benign renal cystic mass: no follow-up
IIF	cystic mass, smooth minimally thickened enhancing wall, or smooth minimal thickening of one or more enhancing septa, or many smooth thin enhancing septa	• minimally thickened wall/septa: 3 mm • many septa: > 4	likely benign renal cystic mass (risk of malignancy: <10 %): follow-up at 6, 12 months and then, annually for 5 years
III	cystic mass, one or more thick enhancing septa/wall, or irregular enhancing wall/septa	• thick wall/septa: > 4 mm • irregular wall/septa: < 3 mm focal or diffuse convex protrusion(s), with obtuse margins with the wall/septa (measurements on CECT, obtained perpendicular to the wall/septa, excluding the wall/septa)	intermediate possibility of malignancy (50 %): referral to a urologist
IV	cystic mass one or more enhancing nodule(s)	• nodule: focal convex protrusion, any size, with acute margins with the wall/septa, or focal convex protrusion > 4 mm, with obtuse margins with the wall/ septa (measurements on CECT, obtained perpendicular to the wall/septa, excluding the wall/septa)	often malignant (90 %): referral to a urologist

uric acid, xanthine and cystine stones. The only exceptions are pure matrix stones and stones in patients on treatment with indinavir, which are of soft-tissue density and therefore, difficult to recognize on CT [7,8,43–47].

CT provides accurate information regarding stone size and location, therefore helping to predict spontaneous stone passage. CT can access the overall stone burden, including number of stones, size and volume, stone density and inner structure, skin-to-stone distance and surrounding anatomy, findings that are useful for the selection of appropriate treatment [7,8,43,44]. The technique helps in the presurgical planning of interventional procedures, such as PCNL and should be used to detect residual stone fragments following PCNL and SWL, as well as to assess the need for a second-look procedure [8]. Associated findings, including signs of acute obstruction, calyceal rupture, fluid collections and/or urinary abnormalities, such as congenital abnormalities, infections and tumors are readily detected [8]. Extraurinary pathologies including gynecologic, gastrointestinal, hepatobiliary, vascular and musculoskeletal conditions mimicking renal colic may be detected in up to one-third of NECTs in patients referred for acute flank pain [48].

The CT protocol for the investigation of acute flank pain includes scanning from the upper pole of the kidneys to the base of the urinary bladder. Axial images can be obtained with 5 mm collimation and then, reconstructed with thinner (1–3 mm) section thickness, allowing the improvement in the detection and characterization of small stones and also the decrease in radiation burden. Coronal MPRs are advocated to assess the entire length of the ureter, helping to detect small stones and enabling the differentiation of urinary stones from calcifications such as phleboliths, calcified plaques and renal parenchymal calcifications. Stone measurements should be performed both in the coronal and axial plane, whilst bone window settings and magnified views are helpful. Intravenous contrast and acquisition of an excretory phase (EP) are recommended in selected patients, such as in cases of uncertainty about whether a calcific density represents a stone or a phlebolith and when stone removal is planned and the anatomy of the renal collecting system needs to be depicted [7,8].

The typical CT sign for ureterolithiasis is the visualization of the calculus within the ureteral lumen. Urinary stones often have a CT density > 200 HU, greater than that of the surrounding soft tissues [8]. Table 2 shows typical CT findings of ureterolithiasis (Figs. 1–3).

Although, NECT has emerged as the standard for imaging acute flank pain, a major concern is the risk of radiation exposure. The American College of Radiology Appropriateness Criteria 2016 state that a LDCT is the examination of choice for assessing patients with suspected urolithiasis, but also considers that KUB combined with US represents an acceptable alternative [7]. A multicenter prospective study, including randomized patients examined for renal colic with CT, radiology-performed US, or point-of-care US reported that US results in lower radiation exposure, without adversely affecting patient-centered outcomes [49]. In pregnant and pediatric patients US should be the modality of first choice. NECT is recommended in cases with less typical clinical presentation, when the initial US findings are inconclusive, in patients with a Body Mass Index (BMI) > 30, in patients who fail to respond to conservative treatment or in those for whom surgery is planned [8,43]. In cases with recurrent symptoms of stone disease, a repeat KUB is recommended for follow-up, if the stone can be observed on KUB [7].

Despite recommendations, recent data suggest that the use of CT in the investigation of acute flank pain continues to increase, raising a concern about radiation exposure [7,8,43,44]. The reported effective radiation dose for NECT is 2.8–13.1 mSv for men and 4.5–18 mSv for women [7]. LDCT (< 3 mSv) and ultra-LDCT (1.9 mSv) can be used to diagnose urolithiasis, with high sensitivity and specificity, although they may not be as effective in detecting stones with sizes < 3 mm, or in patients with a BMI > 30 [6,43]. Dose reduction techniques on NECT include the following: limiting the scanning area from the upper pole of the kidneys to the middle of the pubic symphysis; reducing the tube

ATTACHMENT 12
Purpose of the Project

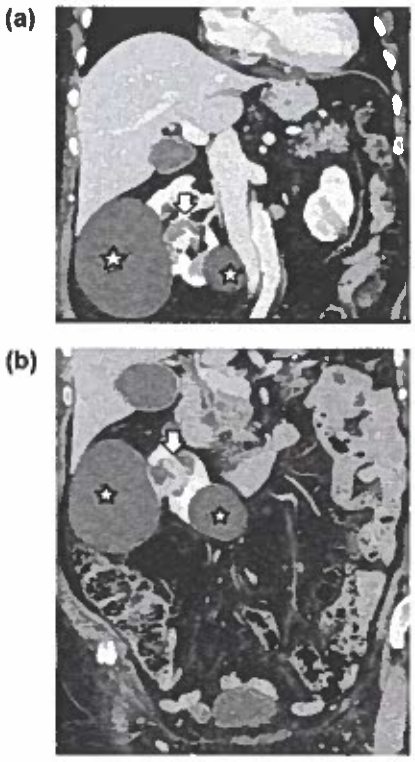

Fig. 4. Bosniak classification, version 2019 class III renal cystic mass. Coronal multiplanar reformations during the (a) corticomedullary and the (b) nephrographic phase show a right-sided renal cystic mass (arrow) in the interpolar region, with thick (≥ 4 mm), contrast-enhancing septa. Two other right renal cysts (stars) are also detected as well-defined, homogeneous lesions, with a water CT density and a smooth, thin, barely enhancing wall (Bosniak classification, version 2019 class I, renal cystic mass)

Table 4
Renal cell carcinoma TNM (tumor-node-metastasis) classification system (IVC: inferior vena cava; LN: lymph node) [61].

T – Primary Tumor
TX primary tumor cannot be assessed
T0 no evidence of primary tumor
T1 tumor ≤ 7 cm in greatest diameter, confined to kidney
T1a tumor ≤ 4 cm
T1b tumor > 4 cm but ≤ 7 cm
T2 tumor > 7 cm in greatest diameter, confined to kidney
T2a tumor > 7 cm but ≤ 10 cm
T2b tumor > 10 cm, limited to the kidney
T3 tumor extends into major veins or perinephric tissues, but not to the ipsilateral adrenal gland and not beyond Gerota's fascia
T3a tumor grossly extends into the renal vein or its segmental (muscle containing) branches, or invades perirenal and/or renal sinus fat, but not beyond Gerota's fascia
T3b tumor grossly extends into infradiaphragmatic IVC
T3c tumor grossly extends into supradiaphragmatic IVC or invades the wall of the IVC
T4 tumor invades beyond Gerota's fascia (including contiguous extension into the ipsilateral adrenal gland)
N – Regional LNs
NX regional LNs cannot be assessed
N0 no regional LN metastasis
N1 metastatic involvement of regional LN (s)
M – Distant metastasis
M0 no distant metastasis
M1 distant metastasis

ATTACHMENT 12
Purpose of the Project

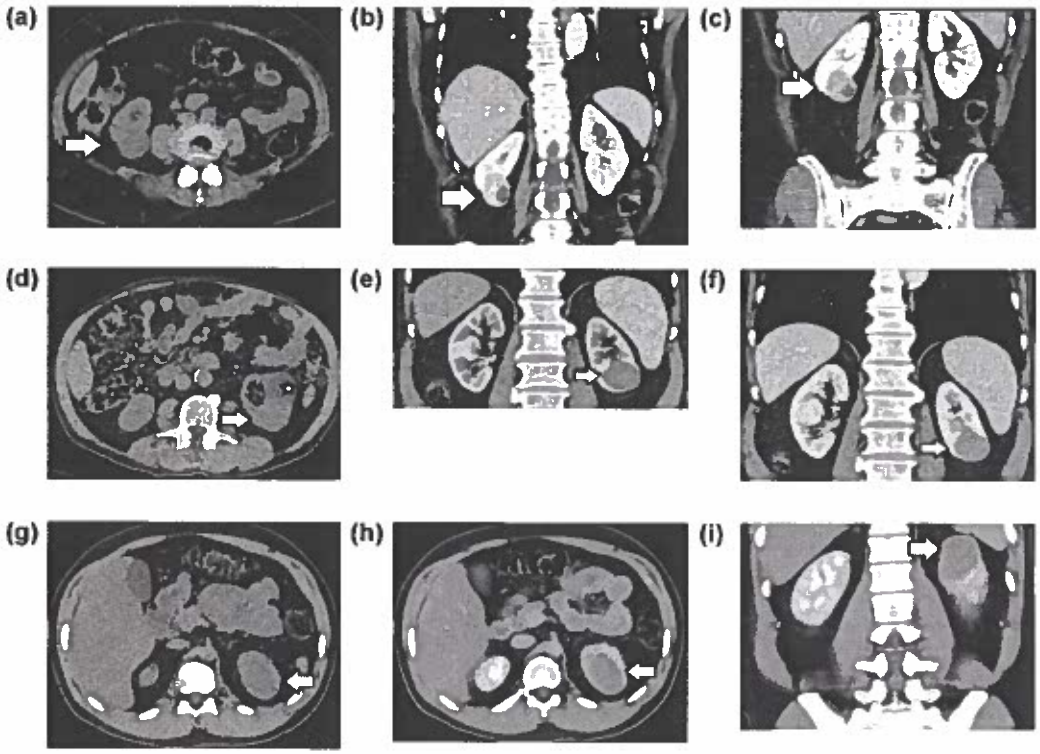

Fig. 5. CT findings of common histologic types of RCC. Clear cell RCC. (a) Axial non-enhanced CT image shows a right lower pole renal tumor (arrow), mainly exophytic and homogeneous, with CT density (30 HU), similar to that of normal renal parenchyma. Coronal reformatted images during the (b) corticomedullary and the (c) nephrographic phase depict early, strong, heterogeneous tumoral enhancement (110 HU, arrow, b), with rapid deenhancement (75 HU, arrow, c). Necrotic part is revealed within malignancy as non-enhancing area. Papillary RCC. (d) Axial non-enhanced CT image demonstrates a homogeneous, slightly hyperdense (40 HU) left renal tumor (arrow), mainly endophytic. A small simple renal cyst (Bosniak classification, version 2019 class I, star) is also seen. Coronal contrast-enhanced images during the (e) corticomedullary and the (f) nephrographic phase depict lower pole left kidney tumor, with well-defined margins, mild contrast enhancement (60 HU, arrow, e), without washout (60 HU, arrow, f). Chromophobe RCC. (g) Transverse non-enhanced CT image shows an upper pole left renal mass (arrow), mainly isodense (35 HU) when compared to normal renal parenchyma. The tumor (arrow) enhances heterogeneously and moderately (70 HU) during the corticomedullary phase (h, axial image), without significant washout (65 HU) during the nephrographic phase (i, coronal plane).

ATTACHMENT 12
Purpose of the Project

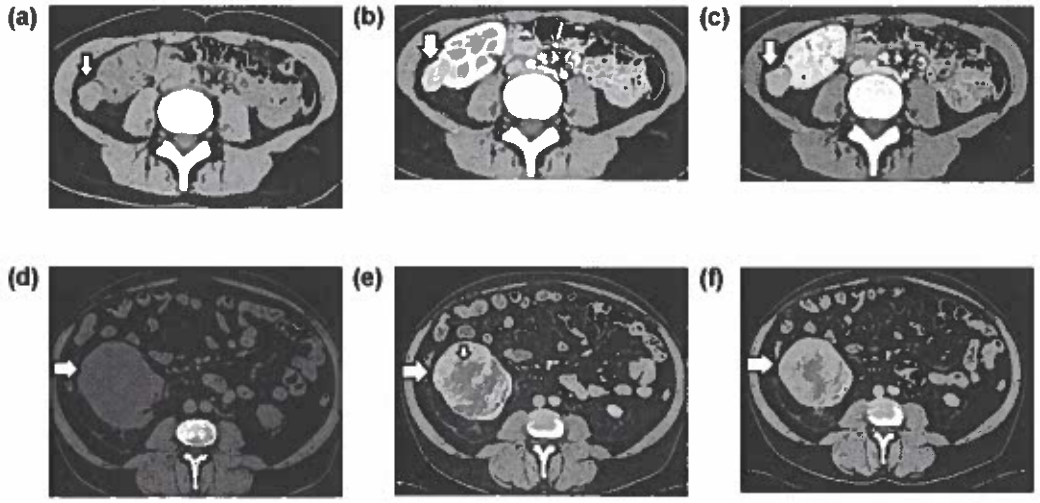

Fig. 6. CT findings of common benign solid renal tumors. Fat-poor AML. Transverse (a) non-enhanced and contrast-enhanced CT images during the (b) corticomedullary and the (c) nephrographic phase depict a small, mainly exophytic right renal mass (arrow). The tumor appears hyperdense on unenhanced images (45 HU), when compared to normal renal parenchyma, with early, marked contrast enhancement, followed by rapid deenhancement. Renal oncocytoma. Transverse (a) non-enhanced and contrast-enhanced CT images during the (b) corticomedullary and the (c) nephrographic phase show a large, well-defined right renal mass (arrow). The tumor is detected heterogeneous, mainly hypodense on unenhanced images. After intravenous contrast medium administration, it reveals an avid, early peripheral enhancement (arrow), followed by moderate washout (arrow) and a large, central non-enhancing stellate scar (small arrow, b).

current and tube voltage; use of 5 mm thickness sections; use of automatic tube current modulation, which allows optimization of radiation dose; and use of iterative reconstruction, which eliminates image noise [7,8,50–52].

4. Renal tumors

Over the last decades, the increased use of cross-sectional imaging, including CT has resulted in a rise in the incidental detection of renal tumors. It is reported that in approximately 14.4 % of CTs, at least one renal mass is incidentally discovered [9,10,53–57].

The first step in the workup of incidentally found renal tumours is to differentiate between benign cysts and solid masses. The majority of renal masses is benign cysts. Renal cystic lesions are usually benign and when malignant, they are less aggressive compared with solid tumors [12]. CT is the most commonly used modality for the assessment of renal cystic tumors, with satisfactory results in the characterization. The 2019 Bosniak classification is recommended for the evaluation of renal cystic masses [12,13]. The updated Bosniak classification introduces specific definitions for individual imaging findings and Bosniak categories, it includes a larger proportion of renal masses found in clinical practice and it enables subgrading in a greater proportion of renal cystic lesions [12,13,58,59]. Table 3 presents the CT features of renal cystic tumors, based on the new classification (Fig. 4) [12].

Most solid renal tumors are malignant and RCC represents the most common histology [53–57]. The main RCC histotypes are the following: clear cell RCC (ccRCC), papillary RCC (pRCC) and chromophobe RCC (chRCC) [60]. Prognosis is mainly related to RCC histologic subtype, tumour stage (Table 4) and nuclear grade [61].

However, not all solid renal tumors are malignant. The reported prevalence of benign pathology between surgically resected solid renal masses is approximately 20 %. Fat-poor angiomyolipoma (fpAML) and renal oncocytoma (RO) comprise most of the benign solid renal tumours. Accurate, noninvasive characterization of renal tumors is therefore important, to determine the best therapeutic planning [9,10,53–57].

CT is often used for the characterization of solid renal tumors [9,10,56]. The technique can provide valuable information in the characterization of RCC histologic types [45,62–65]. Clear cell RCC typically shows avid enhancement in the early phase, when compared to pRCC, chRCC and RO (Fig. 5). CT patterns of enhancement help to differentiate ccRCC from pRCC, chRCC and RO with accuracies of 85 %, 84 % and 77 %, respectively [63].

Angiomyolipomas are benign tumors, derived from the perivascular epithelioid cells (PEComa) family.

Approximately 5 % of AMLs have a nonhomogeneous distribution of fat, defined as < 25 % of fat per high-power field on pathology (fpAMLs). CT does not always permit a reliable characterization of fpAML. However, in the presence of a small, homogeneous solid renal tumor in female patients, detected hyperdense on NECT, with rapid, avid enhancement and washout kinetics, the diagnosis of fpAML should be suggested (Fig. 6a) [53,54,57,66,67]. Renal oncocytoma has variable and nonspecific CT findings that overlap with the characteristics of RCC, especially the chromophobe type (Fig. 6b). Histopathology represents the reference standard [53,54,68,69]. Table 5 shows CT findings that help in the characterization of solid renal tumors.

A core renal CT protocol consists of a NECT scanning and a nephrographic (NGP) phase CECT (Table 6) [53,70]. NECT is important for the detection of macroscopic fat and calcifications and also establishes the baseline CT density of a mass, before contrast medium intravenous administration. NGP is the most sensitive phase for the detection of renal tumors, because almost all renal masses enhance less than normal renal parenchyma. NGP also improves the detection of enhancement and assesses possible tumor thrombus extent into the inferior vena cava (IVC). A corticomedullary phase (CMP) may also be obtained and is useful in sub-typing RCC, assessing renal arterial anatomy and detecting possible renal vein involvement. The addition of an EP is optional and is useful for the detection of urothelial malignancies [53,70]. Thin slices are advocated to minimize partial volume artifacts and to help in the assessment of small renal masses [9,56].

CT with a dedicated renal protocol is usually appropriate for the

ATTACHMENT 12
Purpose of the Project

Table 5
CT findings and clinical features that help in the characterization of solid renal tumors (ccRCC: clear cell renal cell carcinoma; pRCC: papillary renal cell carcinoma; chRCC: chromophobe renal cell carcinoma; fpAML: fat-poor angiomyolipoma; RO: renal oncocytoma; NECT: non-enhanced CT; CMP: corticomedullary phase; NP: nephrographic phase; EP: excretory phase; IVC: inferior vena cava). [1]pRCC has two histologic types: Type 1 and Type 2, the latter associated with a worse prognosis; there are no reliable CT criteria to differentiate between the two types. [2]Central stellate scar: corresponds to a central zone of fibrous connective tissue, with the fibrotic bands radiating towards the periphery of the lesion, closely resembling a star; it is detected as a hypodense area at CT and may demonstrate a stellate or spoke-wheel pattern of enhancement. [3]Segmental enhancement inversion: detected as two parts within a tumor that depict different degrees of enhancement during the CMP, with the relatively highly enhanced part becoming less enhanced during the early EP, whereas, the less enhanced part during the CMP becomes highly enhanced during the early EP. [4]Angular interface: seen in an exophytic renal mass that has a tapering, almost pyramidal interface with a definable apex within the parenchyma.

Histology	Clinical features	Biologic behaviour	CT findings			
			Morphologic features	NECT	CMP	NP
ccRCC	often symptomatic	often diagnosed at advanced stage renal vein or IVC invasion (45 %) worse prognosis, compared to other ROC histotypes	large size exophytic well-defined or ill-defined pseudocapsule rarely multifocal and bilateral (5 %)	heterogeneous central necrosis may have calcifications, haemorrhage or cystic parts macroscopic fat: rare	strong heterogeneous enhancement peak of enhancement perinephric engorged vessels	rapid washout: hypodense compared to normal renal parenchyma
pRCC[1]		venous invasion, only in type 2: advanced stage	small < 3 cm exophytic well-defined (type 1) or ill-defined (type 2: advanced stage) pseudocapsule multifocal and bilateral: more often than ccRCC	homogeneous (type 1) or heterogeneous (type 2: advanced stage) mildly hyperdense (35 HU) calcifications: rare (type 2: advanced stage) macroscopic fat: very rare	weak homogeneous enhancement less than other RCC histotypes	peak of enhancement
chRCC		often diagnosed at early stage: 86 % renal vein invasion: <5%	larger size compared to other RCC histotypes 7.2 cm exophytic completely or predominantly well-defined pseudocapsule central stellate scar[2]: 30–40 %	homogeneous calcifications: 38 % macroscopic fat: very rare	'intermediate' pattern of enhancement: enhances less than ccRCC and more than pRCC	spoke-wheel enhancement[2] segmental enhancement inversion[3]
fpAML	asymptomatic young female sporadic OR in tuberous sclerosis complex (55–90 %) and lymphangiomyomatosis (30–50 %)	benign	< 4 cm angular interface ('ice-cream cone' sign, 'overflowing beer' sign)[4]	homogeneous hyperdense (> 45 HU) hypodense rim macroscopic fat: absent calcifications: absent	homogeneous strong enhancement perinephric engorged vessels: absent	rapid washout
RO	asymptomatic men mean age: 65 years	benign	exophytic completely or predominantly well-defined pseudocapsule 50 % central stellate scar[2]: 33 % (tumors > 2.5 cm)	hypodense perirenal fascia thickening	homogeneous strong enhancement	spoke-wheel enhancement[2] segmental enhancement inversion[3]

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ATTACHMENT 12
Purpose of the Project

Table 5 (*continued*)

Histology	Clinical features	Biologic behaviour	CT findings			
			Morphologic features	NECT	CMP	NP
			rarely multifocal (13 %) and bilateral (4–5 %)			

Table 6
CT renal mass protocol (NECT: non-enhanced CT; CECT: contrast-enhanced CT; NGP: nephrographic phase; CMP: corticomedullary phase; EP: excretory phase) [70].

Scanning	Plane	Area	Reconstruction thickness (mm)	Other parameters
NECT	axial	kidneys	3 mm with or without 50 % overlap	
CECT				• 100–150 ml (300–350 mg of iodine/ml) of contrast medium injection rate: 2–5 ml/sec coronal and sagittal reformations (reconstruction thickness: 3 mm, no overlap)
NP	axial	diaphragm-iliac crests	3 mm with or without 50 % overlap	• delay time: 100-120sec
CMP	axial	kidneys	3 mm with or without 50 % overlap	• delay time: 30-70sec
EP	axial	diaphragm-iliac crests	3 mm with or without 50 % overlap	• delay time: 7–10 min

initial assessment of an indeterminate renal mass, representing an equivalent alternative to magnetic resonance imaging (MRI) and contrast-enhanced US [9,10]. CT density, lesion homogeneity or heterogeneity and contrast enhancement are the key elements for the characterization of renal tumors. The size, location and number of regions of interest (ROIs) used to measure lesion CT density are important. Multiple ROIs should be used, encompassing approximately-two-thirds of the tumor (both on NECT and CECT) in a homogeneous renal mass and placed within different regions in a heterogeneous lesion [9,10].

Contrast enhancement is present, when there is an unequivocal attenuation change of > 20 HU between NECT and CECT and absent, if the change is ≤ 10 HU. Enhancement is considered equivocal, if change is between 10 and 20 HU [9,10,56]. Fig. 7 shows an algorithm for the investigation of a renal mass, incidentally found at CT [9].

4.1. RCC staging

CT of the abdomen represents the diagnostic modality of choice for RCC staging, providing valuable anatomic information, that serve as a roadmap to guide treatment decisions [11,14,15]. RCC can be multifocal, therefore both kidneys should be investigated for the presence of synchronous tumours (Fig. 8) [14].

RCC size is a crucial element of the staging system (Table 4). The maximum tumor diameter should be measured in oblique reformations along the longest dimension of the neoplasm, to minimize overestimation or underestimation of lesion size [15].

RCC pseudocapsule formation is the result of tumor growth, causing compression, ischemia and necrosis of the adjacent renal parenchyma. The presence of pseudocapsule implies early-stage disease. Although less sensitive than MRI, CT often detects tumour pseudocapsule, as a regular, hyperdense or hypodense halo surrounding the neoplasm [71,72].

Thin-section CT improves the detection of PF infiltration, although false-positives are not uncommon, associated with perinephric stranding due to inflammation, oedema, vascular engorgement or fibrosis [14]. The presence of enhancing nodules in the PF is considered highly specific for the diagnosis of PF invasion [73]. The assessment of renal sinus fat invasion is important in candidates for PN, although this sign is often difficult to be accurately diagnosed on CT [14].

CECT has a high sensitivity in detecting venous neoplastic involvement, especially in the main renal vein and the IVC. Enlargement of the vessel, filling defects and enhancing tumour thrombus are signs highly suggestive of venous invasion (Fig. 9). Accurate assessment of the cephalic extent of the IVC thrombus is crucial in preoperative planning. Neoplastic thrombus in the segmental branches of the renal vein and invasion of the IVC wall may be difficult to be assessed on CT [14].

CT has high sensitivity and nearly 100 % negative predictive value in the diagnosis of neoplastic invasion of the neighbouring organs, including the adrenal gland, although the positive predictive value in distinguishing mere abutment from infiltration is low [14]. CT has a 10 % false-negative rate and a 50 % false-positive rate, when using morphologic criteria to diagnose metastatic lymphadenopathy, such as a short-axis diameter >1 cm and disruption of the normal lymph node (LN) architecture [14]. CT represents the examination of choice for the detection of distant metastases. RCC metastatic lesions are often hypervascular and therefore may be better detected in the CMP [14].

5. CT urography

The definition of CTU, as proposed by the European Society of Urogenital Radiology includes a diagnostic examination dedicated for imaging the kidneys, ureters and bladder and involving the use of thin slices, intravenous administration of iodinated contrast medium and imaging in the EP [19]. CTU is recommended for the initial imaging of gross hematuria and for the initial imaging of microhematuria, in patients with risk factors for urologic malignancies [16].

Standard CTU protocol (single-bolus technique) starts with an unenhanced scanning of the urinary tract, to detect stones and to assess the enhancement of renal/ureteral/bladder soft tissue masses. After the bolus injection of intravenous contrast, three or four contrast-enhanced phases are obtained in the arterial (CMP), NGP and EP. The split-bolus technique has also been used, including the administration of two separate injections of intravenous contrast and the acquisition of a combined NGP/EP. Although this protocol results in reduced radiation dose, decrease in sensitivity for the detection of subtle urothelial lesions and small RCCs as well as inadequate tumor staging have been reported [19–22,74–77].

Incomplete distention and opacification of the ureters (particularly the distal parts) represent the biggest CTU challenge for radiologists. Several ancillary techniques have been proposed to maximize the distention of the collecting system, such as intravenous administration of diuretics, oral or intravenous hydration, prone position and

ATTACHMENT 12
Purpose of the Project

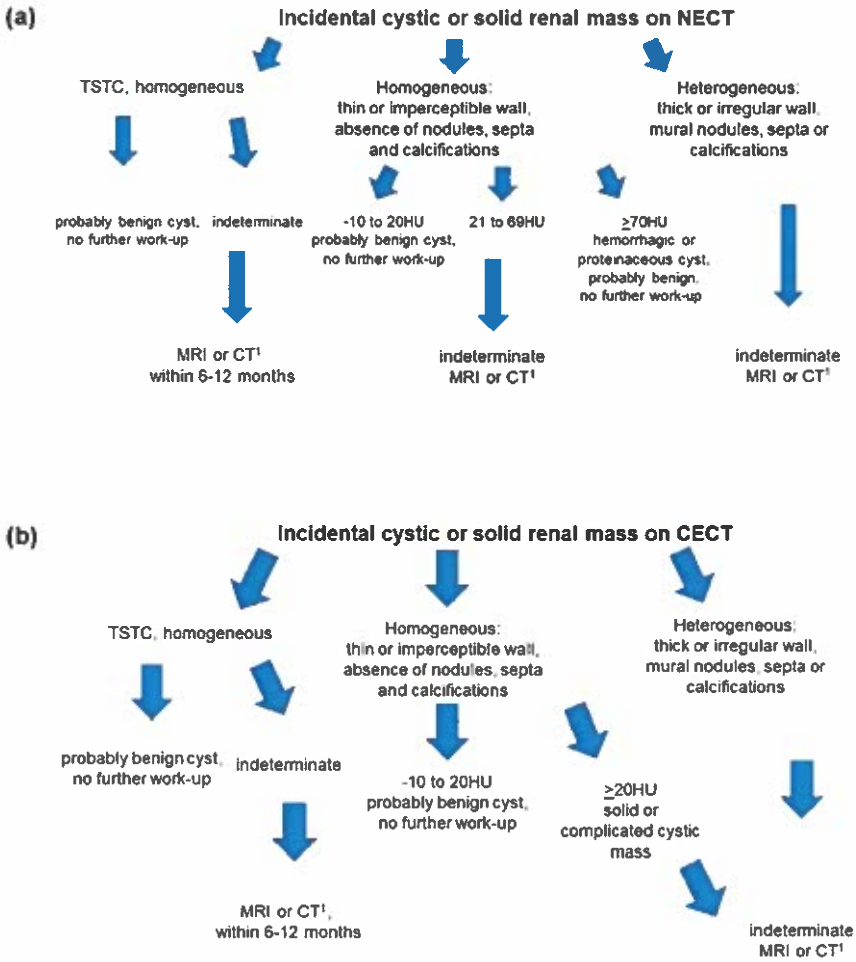

Fig. 7. Flowchart for the assessment of a cystic or solid renal tumor, incidentally found at (a) non-enhanced and (b) contrast-enhanced CT (NECT: non-enhanced CT; TSTC: too small to characterize; CECT: contrast-enhanced CT). [1]CT and MRI with and without intravenous contrast medium represent equivalent alternatives; MRI is preferred for the assessment of small renal tumors (< 1.5 cm); if old examinations are available, any renal mass without change in imaging features or with an average growth of < 3 mm per year for at least 5 years does not need further work-up.

ATTACHMENT 12
Purpose of the Project

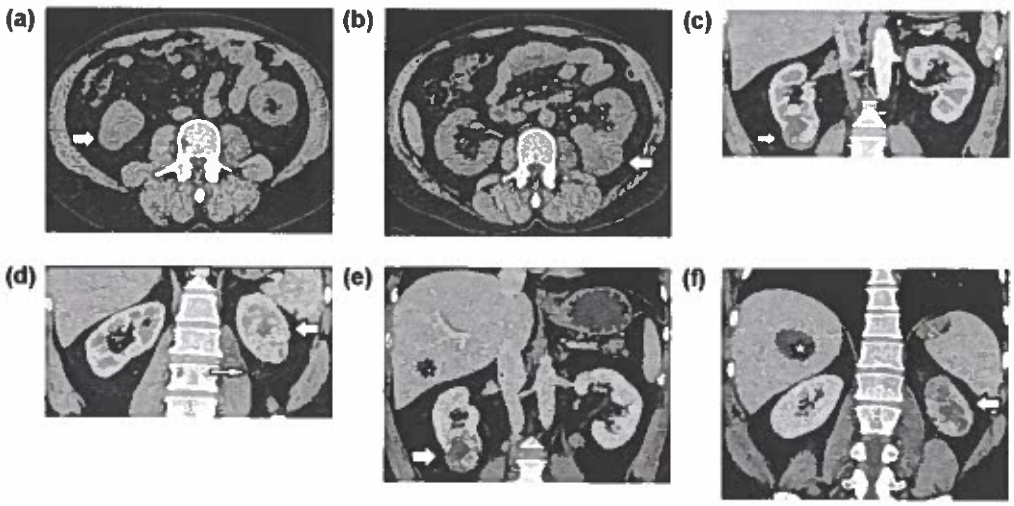

Fig. 8. Synchronous bilateral clear cell RCCs. Axial (a, b) non-enhanced CT images show bilateral renal masses (arrows), mainly isodense to normal renal parenchyma, both deforming kidney contour. Coronal reformations during the (c, d) corticomedullary and the (e, f) nephrographic phase demonstrate renal tumors (arrows) with strong, early, heterogeneous enhancement and rapid washout, findings that are strongly suggestive of clear cell RCCs. Nonenhancing parts within the neoplasms correspond to areas of necrosis on histology. Note, small collateral vessels in the perirenal space (long arrow, d), a finding also suggestive of the clear cell variant. Sporadic bilateral synchronous RCCs are rare, reported in less than 2% of patients with RCCs. Simple liver cyst (asterisk, e, f).

abdominal compression [20,21,74–79]. Among these techniques, hydration has been shown to be the simplest means to achieve maximal distension of the collecting system and opacification of the ureters [20,21].

CTU data interpretation requires careful assessment of the source axial images in combination with multiplanar and 3D reconstructions. Maximum-intensity projection (MIP) reconstructions are particularly helpful, allowing a satisfactory global overview of the renal collecting systems and ureters and better assessment of subtle areas of urothelial thickening and strictures (Fig. 10). Evaluation of the EP data using wide-window settings is also recommended to better visualize caliceal details and small filling defects within the collecting system [20,21].

5.1. *Upper tract urothelial carcinoma*

Urothelial carcinomas are the 6th most common type of cancer in developed countries. Notably 90–95 % of these tumors involve the bladder wall and only 5–10 % the upper urinary tract. Patients usually present with gross or microscopic hematuria [80,81].

Pelvicaliceal tumors are approximately twice as common as ureteral tumors and multifocal neoplasms are found in 10–20 % of cases. When the ureter is affected, the most commonly involved part is the distal third. Following treatment, approximately 40 % of patients with UTUCs develop a metachronous tumor in the urinary bladder and 2–5 % in the contralateral upper tract [20,80].

CTU has the highest accuracy for the diagnosis and staging of UTUC [16,80,81–84]. According to a recent systematic meta-analysis, CTU represents the technique of choice for the investigation of UTUCs, with 92 % sensitivity and 95 % specificity [84].

The main CTU appearances of UTUCs include an area of focal, concentric or eccentric urothelial thickening, with contrast enhancement, a soft tissue mass and an infiltrative mass. Mass-like UTUCs are of soft-tissue density on NECT, with lower attenuation compared to stones and blood clots, showing early moderate contrast enhancement and detected as filling defects in the EP (Fig. 11, 12). These tumors may show granular, linear or punctate calcifications (Fig. 11b). Some UTUCs present as locally aggressive, infiltrative masses, distorting or obstructing the collecting system or the ureter, with upstream dilatation. Direct infiltration of the renal parenchyma by the tumor is seen as kidney enlargement, heterogeneity and hypoenhancement of the parenchyma, but with preservation of the reniform shape of the organ (Fig. 11h-j, 13) [20–21,82,85,86]. Table 7 presents typical CTU findings of UTUCs and common mimickers.

Subtle urothelial thickening, without mass effect or associated urinary obstruction may be difficult to detect on CTU. Meticulous assessment for subtle hydronephrosis and/or hydroureter or asymmetry in ureteral dilatation (Fig. 10), particularly focused on the transition point between the dilated portion and the normal caliber ureter may indicate the presence of a small ureteral malignancy [21,80].

Accurate staging of UTUC is crucial in planning treatment (Table 8) [80,87]. Kidney-sparing surgery has been proposed for low-risk UTUCs, including unifocal tumors, of maximal diameter less 2 cm, noninvasive CTU findings and low-grade on cytologic or biopsy specimens [80]. When a fat plane or a layer of excreted contrast is intervened between the mass and renal parenchyma, the tumor is characterized as of early-stage (T1 or T2), including neoplasms that do not invade beyond muscularis. Loss of renal sinus fat or abnormal enhancement of adjacent renal parenchyma are signs of invasive disease (T3). Direct invasion of

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Purpose of the Project

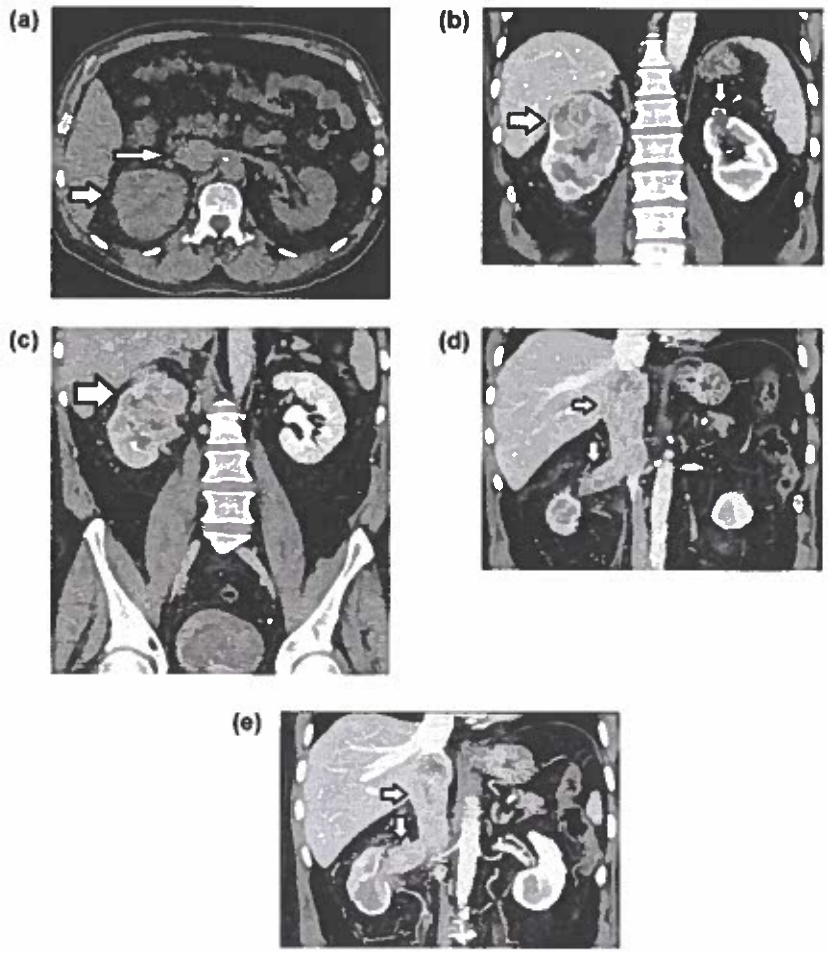

Fig. 9. Clear cell RCC with neoplastic involvement of the ipsilateral renal vein and the inferior vena cava (T3b). (a) Axial non-enhanced CT image shows heterogeneous right renal mass (arrow) causing obliteration of the renal sinus. Enlargement of the inferior vena cava (long arrow) is also seen. Coronal reformations during the (b) corticomedullary and (c) the excretory phase depict expanding right renal mass (arrow) heterogeneously enhancing and invading the pelvicalyceal system. A small renal cystic mass with peripheral calcifications (Bosniak classification, version 2019 class II renal cystic mass, small arrow, b) is detected in the upper pole of the left kidney. Coronal (d) multiplanar reformatted and (e) three-dimensional reconstructed maximum-intensity projection, MIP images during the corticomedullary phase show right renal vein and inferior vena cava expanding thrombus, heterogeneously enhancing (arrows). Accurate preoperative evaluation of extent of the neoplastic thrombosis of the inferior vena cava is important for planning the appropriate surgical approach for thrombectomy.

ATTACHMENT 12
Purpose of the Project

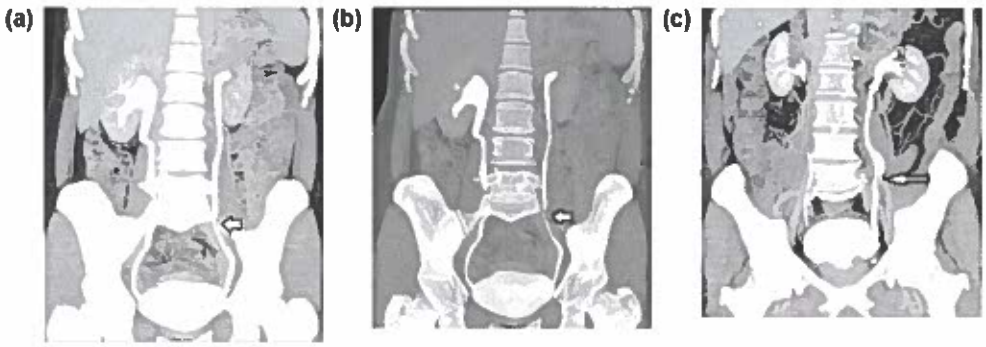

Fig. 10. CTU findings of ureteral tumors in two patients. Coronal MIP reformations of the excretory phase, using (a) soft-tissue and (b) bone-window settings show a small irregular ureteral narrowing (arrow) involving the middle third of the left ureter. (c) Coronal MIP reformatted image of the excretory phase in another patient reveals a subtle narrowing (arrow) of the middle third of the left ureter, causing proximal ureteral dilatation and mild left hydronephrosis. MIP reformations are particularly useful in detecting minimal ureteral narrowing and/or asymmetric hydronephrosis/hydroureter as signs of a small ureteral urothelial tumor.

the perinephric fat or adjacent organs defines T4 stage [20,21,87].

5.2. *Urinary bladder carcinoma*

Cystoscopy is mandatory for the diagnosis of BC [23]. Men with a bladder tumor diagnosed by any imaging technique may avoid flexible cystoscopy and go directly to rigid cystoscopy and transurethral resection (TURB), for histological diagnosis and resection of the bladder [23]. In 30 % of patients with BC, synchronous multifocal tumors are detected (Fig. 14).

For staging, the tumor-node-metastasis (TNM) classification is recommended (Table 9) [23,87]. Approximately 75 % of patients present with NMIBC, including tumors confined to the mucosa (stage Ta, Tis: *in situ*) or submucosa (T1). NMIBCs are treated by TURB, in combination with intravesical instillations [23,88]. Due to the fact that the incidence of synchronous UTUCs is low (1.8 %) in these patients, CTU is recommended in selected cases, including BCs involving the trigone, multiple or high-risk tumors [23,88].

CT of the abdomen is recommended for the evaluation of locally advanced MIBC stage and tumor spread to LNs or distant organs. CTU is the preferred study for the assessment of synchronous UTUCs [2,89–92].

BC typically enhances more intensely than the adjacent normal bladder wall on CT and can be detected as polypoid mass, a broad-based, plaque-like area of wall thickening or an infiltrative, diffuse lesion (Figs. 14-16) [90,93]. The sensitivity and specificity of CTU in the detection of primary and recurrent bladder BC has been reported to be 93 % and 99 %, respectively [90,95]. Optimal bladder distention and careful assessment of the bladder wall, both on axial images and MPRs in the coronal and sagittal planes are essential for BC detection. CT is limited in the detection of neoplasms at the bladder neck and flat, sessile lesions [85]. In addition, Tis cannot be detected based on imaging [23].

Regarding local staging, CT is sensitive in identifying tumors that have macroscopically invaded the perivesical fat (T3b) and/or adjacent organs (T4) [23,89–99]. CT accuracy in assessing extravesical tumor extension varies between 55 % and 92 %, increasing with more advanced stages [23]. Perivesical invasion is diagnosed in cases of overt growth of BC beyond the outer margin of the bladder wall and/or in the presence of an irregular interface between tumor and perivesical fat (Fig. 16) [90,93]. Stranding of the perivesical fat is often found to coexist. CT should be best obtained prior to TURB, to avoid postbiopsy changes in the perivesical fat, closely resembling extravesical tumor extension [89].

The accuracy of CT in differentiating NMIBC from MIBC is limited. This is because the layers of the bladder wall are invisible on CT and the attenuation of BCs and bladder wall are often similar [23,90,97]. Retraction of the bladder wall and/or hydronephrosis are indirect CT signs of locally invasive tumors (Fig. 16) [90].

The accuracy of CT in the diagnosis of metastatic lymphadenopathy in BC varies from 54 to 86 % [97]. A short-axis diameter > 8 mm for pelvic LNs and > 10 mm for abdominal LNs is considered pathologic [23,90,97]. The recently introduced 'Node Reporting and Data System (Node-RADS)' standardizes the report of metastatic involvement of regional and distant LNs, based on size and configuration, on cross-sectional imaging, including CT. This system aims to improve the communication with the referring physicians and to increase the consensus among radiologists for primary staging and in response assessment settings [100].

6. CT advances

Dual-energy, multi-energy and spectral CT post-processing techniques, including the creation of virtual unenhanced images and iodine density maps can help in the characterization of indeterminate renal tumors and urinary calculi composition and reduce radiation exposure by eliminating the NECT scanning [25–31]. Through mathematical extraction of the spatial distribution of signal-intensities and pixel-interrelationships, CT-based radiomics quantify hidden textural information in a renal mass, showing promise in the characterization of renal tumors [32–35].

7. Conclusions

CT of the abdomen often represents the examination of choice for the comprehensive evaluation of many urinary tract diseases, helping to plan tailored treatment. Optimal CT protocol is essential for accurate data interpretation.

ATTACHMENT 12
Purpose of the Project

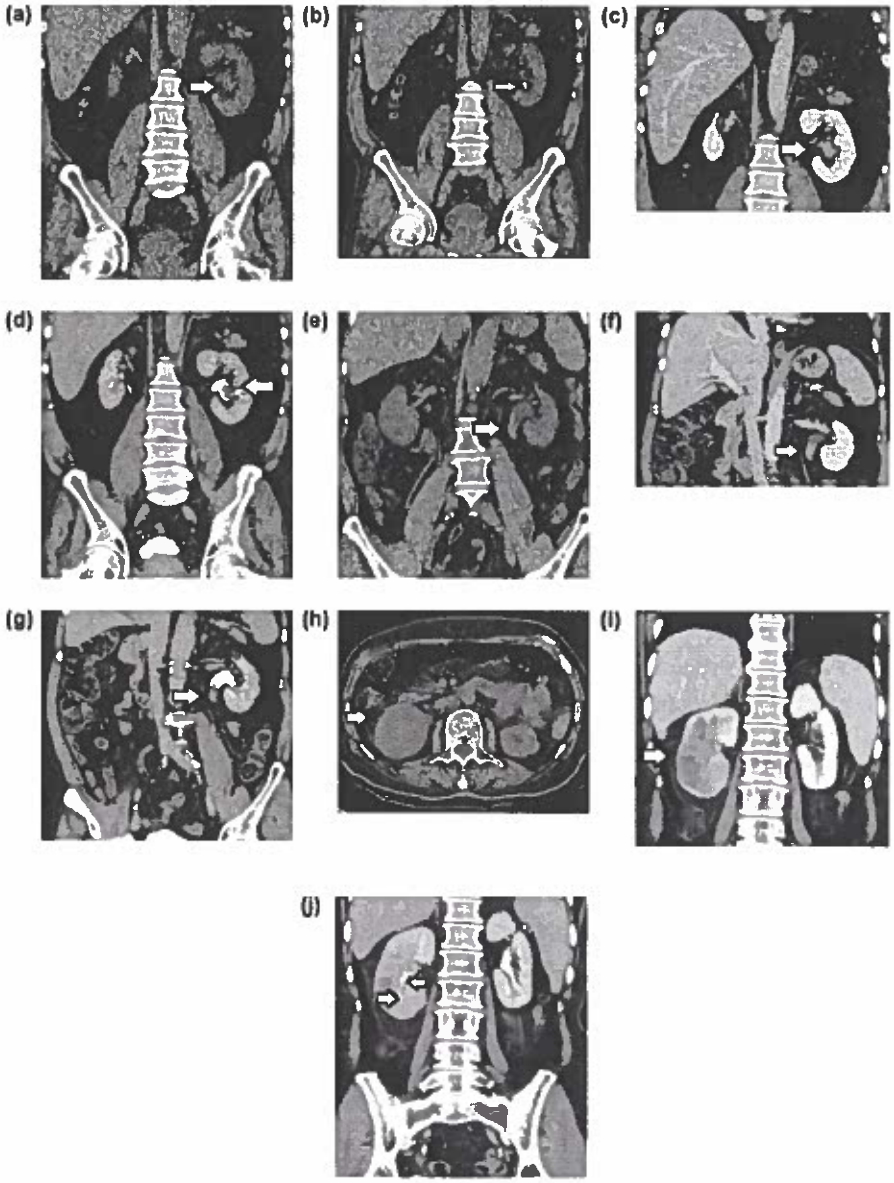

Fig. 11. CTU findings of upper tract urothelial tumors in three patients. (a,b) Coronal reformatted non-enhanced CT images depict a soft-tissue mass (arrow) of the left lower calyx. The lesion contains small calcifications (arrow, b). Coronal reformatted contrast-enhanced images show tumor (arrow) as a moderately enhancing mass in the (c) nephrographic phase and as an ill-defined filling defect (d) in the excretory phase. Urothelial carcinoma of the renal pelvis. Coronal (e) non-enhanced and contrast-enhanced CT images during the (f) nephrographic and the (g) excretory phase. The tumor (arrow) is detected as a soft-tissue mass on unenhanced images, isodense to normal renal parenchyma, moderately enhancing and as a filling defect with irregular margins in the excretory phase. Infiltrative upper tract urothelial tumor. (h) Axial non-enhanced CT image demonstrates right kidney enlargement and heterogeneity (arrow), with effacement of the renal sinus fat and perinephric stranding. Coronal reformations during the (i) nephrographic and the (j) excretory phase show renal malignancy (arrow) inhomogeneously enhancing and invading both the collecting system (arrows, c) and the renal parenchyma. Note, the preservation of the reniform shape of the diseased kidney, a finding suggestive of the urothelial origin of the neoplasm.

ATTACHMENT 12
Purpose of the Project

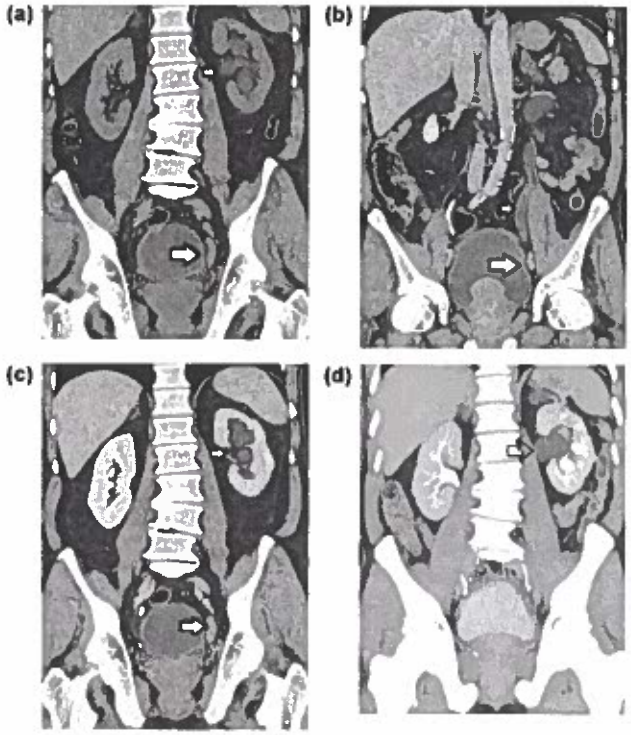

Fig. 12. Ureteral urothelial tumor. Coronal multiplanar reformations of the (a) non-enhanced scanning, the (b) nephrographic and the (c) excretory phase reveal a soft-tissue mass (arrow) in the distal third of the left ureter, moderately enhancing. The mass causes upstream ureteral dilatation, left hydronephrosis (small arrow, a, c) and delay in the excretion by the ipsilateral kidney. Note, diffuse mucosal enhancement of the proximal part of the left ureter (small arrow, b), a finding suggestive of coexisting inflammation. Benign hyperplasia of the prostate is also seen

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Purpose of the Project

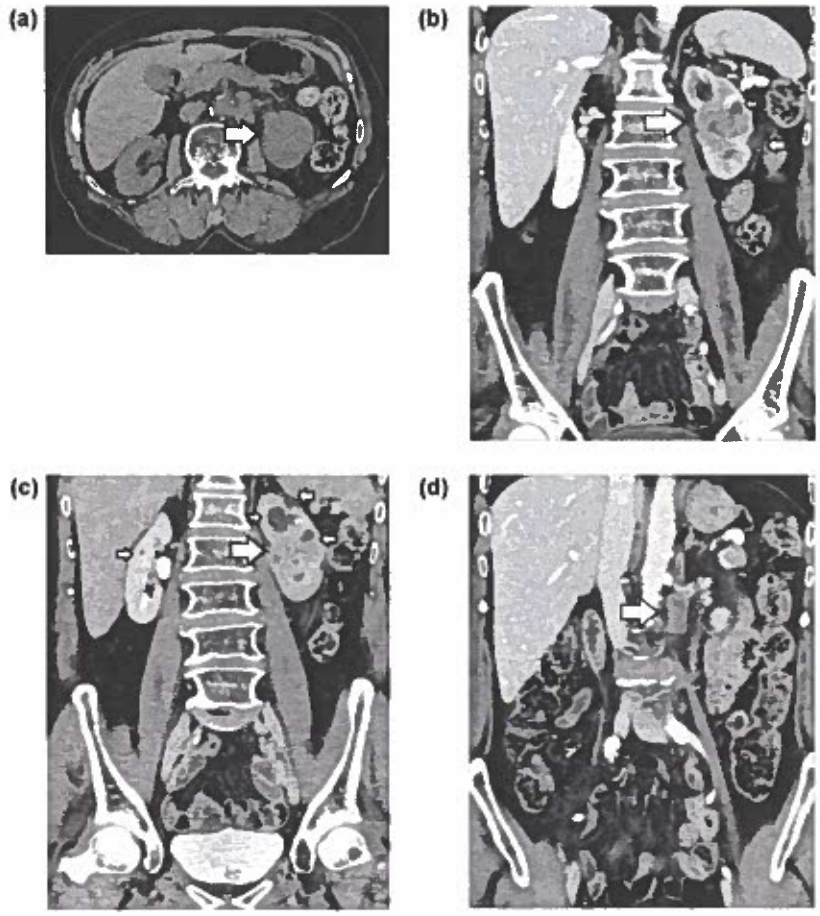

Fig. 13. Upper tract urothelial tumor with metastatic retroperitoneal lymphadenopathy. (a) Transverse non-enhanced CT image shows heterogeneous left renal mass (arrow) with obliteration of the renal sinus. Left perinephric stranding is also seen. Coronal reformatted images during the (b) nephrographic and the (c) excretory phase depict urothelial malignancy (arrow) inhomogeneously enhancing and invading the pelvicalyceal system. Note, the absence of renal contour deformity by the tumor. (d) Coronal reformation during the nephrographic phases demonstrates enlarged, heterogeneously enhancing left paraaortic lymph nodes (arrow). Small bilateral simple renal cysts (Bosniak classification, version 2019 class I, small arrows, b, c) are also seen.

ATTACHMENT 12
Purpose of the Project

Table 7
CT features of upper tract urothelial carcinomas and common mimickers [22] (NECT: non-enhanced CT; NGP: nephrographic phase; CMP: corticomedullary phase; EP: excretory phase; UTUC: upper tract urothelial carcinoma; Tbc: tuberculosis; RCC: renal cell carcinoma). [1] Clinical, laboratory findings and follow-up CT help in differential diagnosis. [2] Differential diagnosis may be difficult. Lesion multiplicity favors the diagnosis of Tbc. [3] Differential diagnosis is difficult. Lesion heterogeneity and presence of fever favors the diagnosis of pyeloureteritis cystica.

CT findings	NECT	CMP/NGP	EP
UTUT	• soft-tissue mass (8-30 HU), may have calcifications	mild to moderate, early enhancement	filling defect, smooth or ill-defined margins
	• concentric or eccentric wall thickening	enhancement	luminal narrowing
	• infiltrative mass, heterogeneous, **preservation of the reniform kidney shape**	heterogeneous, mild to moderate enhancement, hypoenhancement of the renal parenchyma	distortion or obstruction of the renal collecting system
	+ upstream dilatation, reduced nephrographic effect, delayed contrast medium excretion		
Mimickers			
• blood clot	hyperdense (40-80 HU)	absence of enhancement	entirely surrounded by opacified urine
• inflammation[1]	circumferential, symmetric wall thickening, smoothly margined, symmetric, homogeneous attenuation of the surrounding fat	diffuse enhancement	
• hypertrophied renal papilla			filling defect, smooth margins, preservation of forniceal shape, multiplicity
• renal papillary necrosis		absence of enhancement	central erosion of the papilla, filled with opacified urine ("teardrop-shaped" cavity) OR erosion of the calyceal fornices, filled with opacified urine ("lobster-claw" calyx) [early phase] filling defect, surrounded by contrast medium in the excavated calyx ("signet ring" sign); caliceal abnormality extends proximal to the interpapillary line, opacified urine located deep into the medulla vs UTUT: caliceal abnormality extends toward renal pelvis
• Tbc[2]			
	tuberculoma: soft-tissue mass, hypodense center irregular wall thickening	enhancement	signs of papillary necrosis, caliceal deformity ("moth-eaten" calyx) [early phase], direct communication with calyces, irregular strictures and caliectasis OR amputation of the calyces ("rose-thorn" shape)
	parenchymal destruction and calcification [chronic phase]		
• fibroepithelial polyp	soft-tissue mass, elongated shape, smooth margins, lesion movement between images aside from attachment zone	enhancement	filling defect, entirely surrounded by contrast medium, except for the attachment site of the stalk
• suburothelial hemorrhage	diffuse, renal sinus wall thickening, hyperdensity		luminal narrowing
• pyeloureteritis cystica[3]			multiple small filling defects (few mm)
• retroperitoneal fibrosis	soft-tissue mass, enveloping the aorta, obscuration of fat planes	enhancement	medial ureteral displacement
• RCC	expansile growth, well-defined or ill-defined margins	heterogeneous enhancement	
• renal lymphoma	homogeneous, soft-tissue mass	mild enhancement	absence of collecting renal system distortion or hydronephrosis

Table 8
Upper tract urothelial carcinoma TNM (tumor-node-metastasis) classification system (PF: perinephric fat; LN: lymph node) [87].

T – Primary Tumor
TX primary tumor cannot be assessed
T0 no evidence of primary tumor
Ta non-invasive papillary carcinoma
Tis carcinoma *in situ*
T1 tumor invades subepithelial connective tissue
T2 tumor invades muscularis
T3 (Renal pelvis): tumor extends beyond muscularis into peripelvic fat or renal parenchyma (Ureter): tumor extends beyond muscularis into periureteric fat
T4 tumor invades contiguous organs or through the renal parenchyma the PF
N – Regional LNs
NX regional LNs cannot be assessed
N0 no regional LN metastasis
N1 metastasis in a single LN < 2 cm in greatest diameter
N2 metastasis in a single LN > 2 cm, or multiple LNs
M – Distant metastasis
M0 no distant metastasis
M1 distant metastasis

ATTACHMENT 12
Purpose of the Project

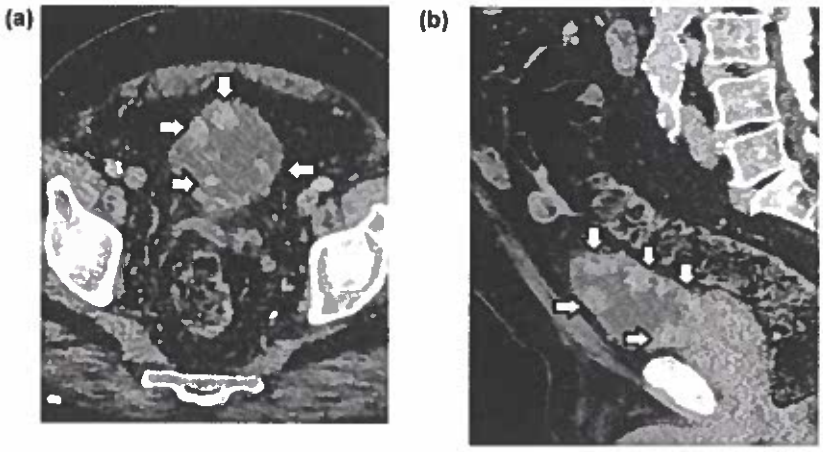

Fig. 14. Multiple synchronous bladder carcinomas. Multiplanar reformations of contrast-enhanced CT images (portal phase) in (a) axial and (b) sagittal planes demonstrate multiple bladder tumors (arrows) as polypoid, contrast-enhanced masses

Table 9
Bladder carcinoma TNM (tumor-node-metastasis) classification system (LN: lymph node) [87].

T – Primary Tumor
TX primary tumor cannot be assessed
T0 no evidence of primary tumor
Ta non invasive papillary carcinoma
Tis carcinoma *in situ*
T1 tumor invades subepithelial connective tissue
T2 tumor invades muscularis
T2a tumor invades superficial muscle (inner half)
T2b tumor invades deep muscle (outer half)
T3 tumor invades perivesical tissue
T3a microscopically
T3b macroscopically (extravesical mass)
T4 tumor invades any of the following: prostate stroma, seminal vesicles, uterus, vagina, pelvic wall, abdominal wall
T4a tumor invades prostate stroma, seminal vesicles, uterus or vagina
T4b tumor invades pelvic wall or abdominal wall
N – Regional LNs
NX regional LNs cannot be assessed
N0 no regional LN metastasis
N1 metastasis in a single LN in the true pelvis (hypogastric, obturator, external iliac, or presacral)
N2 metastasis in multiple regional LNs in the true pelvis (hypogastric, obturator, external iliac, or presacral)
N3 metastasis in a common iliac LN(s)
M – Distant metastasis
M0 no distant metastasis
M1 distant metastasis
M1a non regional LNs
M1b other distant metastasis

NECT is used as the first-line imaging modality for suspected urolithiasis in an emergency setting. The technique is highly accurate in the detection of urinary calculi, providing valuable information to the urologists regarding spontaneous stone passage or the selection of the appropriate treatment strategy. However, CT exposes the patient to ionizing radiation and therefore, combined KUB and US may be used as an alternative, while LDCT is recommended in selected patients.

Characterization of renal tumors is critical to determine the best therapeutic approach and to improve patient survival. CECT is the most commonly used method to evaluate indeterminate renal masses, playing an important role in the characterization of both solid and cystic tumours. Staging of a primary renal tumour is typically performed with CECT, providing important preoperative anatomic information to the surgeon.

CTU remains the standard of imaging for the investigation of macroscopic haematuria and microscopic haematuria, in the presence of risk factors for urologic malignancies. The technique is highly recommended for the detection and staging of UTUCs.

CECT of the abdomen is often used for staging BC, with satisfactory results in advanced tumours.

CT-based innovative approaches, including dual-energy, multi-energy, spectral CT and CT-based radiomics might improve the diagnostic efficacy of the technique in the investigation of the urinary tract.

ATTACHMENT 12
Purpose of the Project

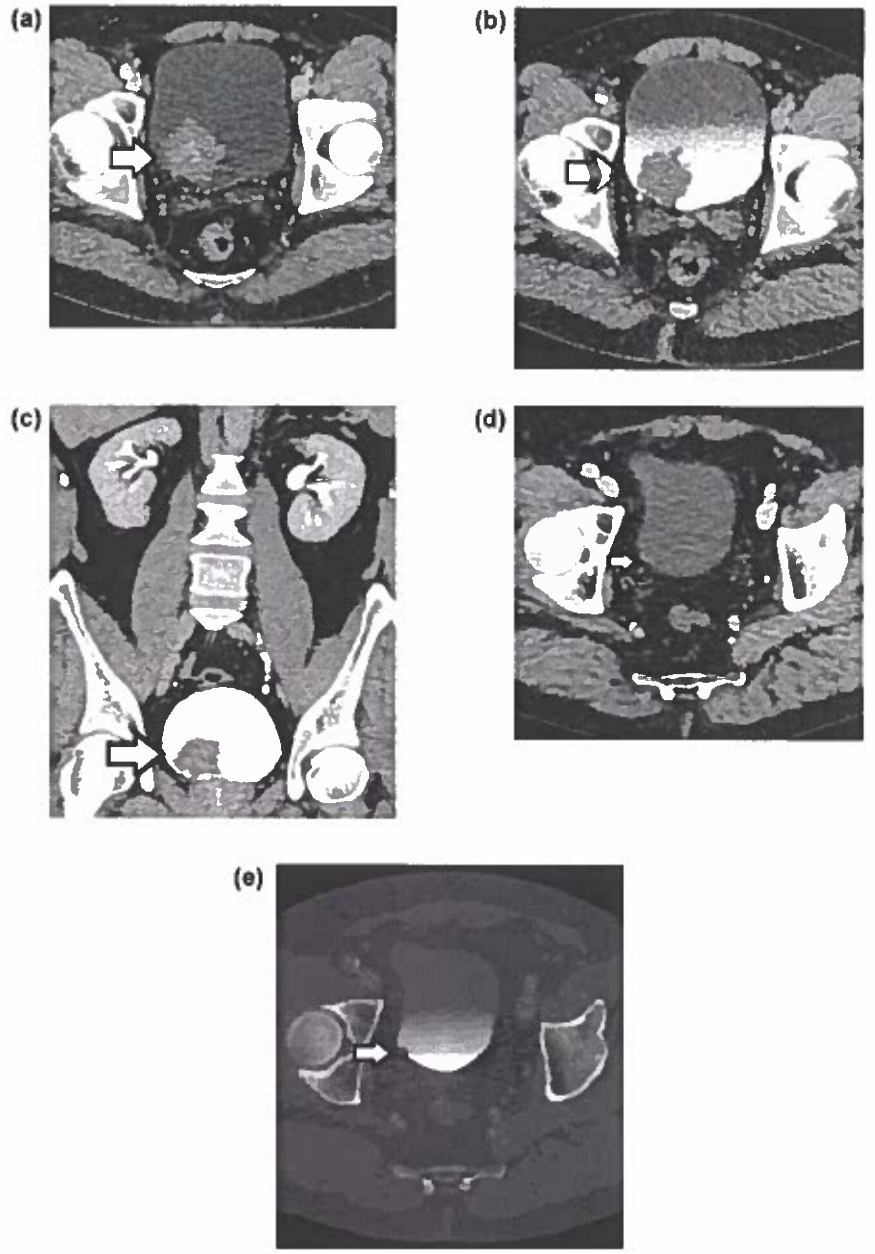

Fig. 15. CTU findings of bladder carcinomas in two patients. (a) Axial contrast-enhanced CT reformation during the corticomedullary portal phase, (b) axial and (c) coronal reformations during the excretory phase show a large polypoid tumor (arrow) in the right posterior bladder wall, close to the ipsilateral ureterovesical junction. The mass (arrow) has an irregular surface, enhances heterogeneously and is detected as a filling defect in the excretory phase. Transverse contrast-enhanced reformations during the (d) corticomedullary portal and the (e) excretory phase (wide-window settings) in another patient. A small bladder mass (arrow) is detected in the right posterolateral bladder wall. The tumor is barely seen as a contrast-enhancing lesion in the portal phase, better appreciated as a filling defect in the excretory phase, using bone window settings. Assessment of the excretory phase data with wide window settings is extremely helpful to better visualize small filling defects within the dense excreted contrast medium in the urinary collecting system.

ATTACHMENT 12
Purpose of the Project

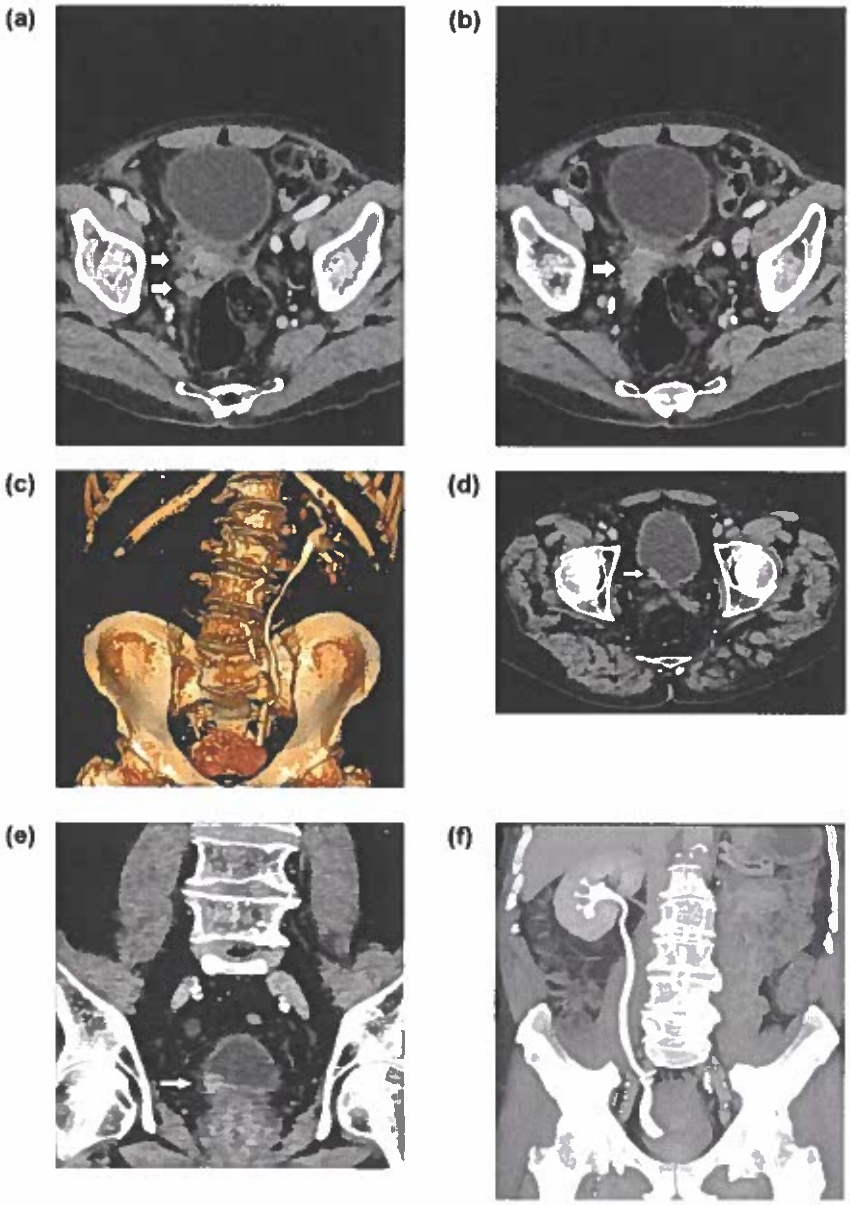

Fig. 16. CT findings of muscle-invasive bladder carcinomas in two patients. (a,b) Axial contrast-enhanced CT images during the portal phase show invasive carcinoma of the right posterolateral bladder wall (arrow) as an area of focal wall thickening and contrast enhancement with overt perivesical extension and invasion of the rectum. The tumor also invades the right ureterovesical junction, resulting in ureteral dilatation, right hydronephrosis and delay in the excretion of the contrast medium by the ipsilateral kidney, as seen in (c) coronal 3D volume-rendered reconstruction of the excretory phase. (d) Axial and (e) coronal contrast-enhanced CT images during the portal phase in another patient depict a nodular, contrast-enhancing bladder tumor (arrow), measuring 12x10 mm in the area of the right ureterovesical junction. The neoplasm causes proximal ureteral dilatation and right hydronephrosis, as demonstrated on the (f) coronal 3D MIP reconstructed image of the excretory phase.The presence of hydronephrosis is strongly predictive of extravesical tumor involvement

ATTACHMENT 12
Purpose of the Project

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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ATTACHMENT 12
Purpose of the Project

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ATTACHMENT 12
Purpose of the Project

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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 treatments. The Applicant seeks 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 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: 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 (LINAC and CT Machine,)	**1,574**	**Total: 4,200** 2,400 GSF Per Unit (Accelerator); 1,800 GSF Per Unit (CT Scan)	**-2,626**	**YES**

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.

Both the LINAC and CT Scan will be utilized at the facility to provide both imaging and radiation treatments to patients. To determine the projected utilization of the new equipment, the Applicants have reviewed their historical utilization for referrals to existing facilities that have similar equipment.

On average during the past calendar year, UroPartners and affiliated physicians have sent 3,000 patients for scans and treatment. There is an expectation that with the new technological advance in medical condition diagnosis and the wider variety of conditions that can be treated with this equipment that there will be an increase in historical volumes over time.

UTILIZATION					
	DEPARTMENT / SERVICE	**HISTORICAL UTILIZATION (PATIENT DAYS) (TREATMENTS) ETC.**	**PROJECTED UTILIZATION**	**STATE STANDARD**	**MEET STANDARD?**
YEAR 1	Diagnostic / Interventional Radiology	3,000 procedures (Accelerator) 3,000 procedures (CT Scan)	3,000 procedures (Accelerator) 3,000 procedures (CT Scan)	7,500 procedures (Accelerator) 7,000 (CT Scan)	YES
YEAR 2	Diagnostic / Interventional Radiology	3,000 procedures (Accelerator) 3,000 procedures (CT Scan)	3,000 procedures (Accelerator) 3,000 procedures (CT Scan)	7,500 procedures (Accelerator) 7,000 procedures (CT Scan)	YES

ATTACHMENT 31
77 Ill. Admin. Section 1110.270- Necessary Expansion (c)(2)

The proposed project is a necessary expansion of the Advanced Radiation Center of Chicago's treatment capabilities to meet patient service demand for specialized radiation oncology care. As discussed in the Purpose of Project section, the Facility serves a high-volume patient population requiring timely access to advanced radiation therapy, and the proposed equipment will both replace deteriorating technology and expand the scope of services available to patients within the Service Area. This section documents the basis for the expansion through historical utilization data, evidence of changes in industry standards, changes in the scope of services offered, and the absence of licensure or code deficiency citations.

The physicians who will utilize the Advanced Radiation Center of Chicago have experienced sustained and growing demand for radiation therapy services over the last several years. The site's existing LINAC has maintained consistently high utilization, reflecting the substantial need for radiation oncology services among patients in northern Cook County and surrounding communities.

The consistent utilization demonstrates that the Facility was operating at or near capacity with its existing equipment. Moreover, UroPartners' network of over 90 providers generates a steady and growing volume of referrals for radiation therapy, particularly for prostate cancer and other urologic malignancies. The current equipment configuration limits the Facility's ability to accommodate this demand efficiently, as the aging LINAC's increasing downtime and longer treatment delivery times reduce effective throughput. The proposed Varian Ethos system's ability to deliver precise radiation treatments in approximately 15 minutes per session combined with its adaptive workflow will increase the Facility's effective daily treatment capacity and reduce patient wait times for initiation of therapy.

Additionally, the proposed expansion of services to include adaptive radiation therapy for breast, lung, gastrointestinal, gynecological, head and neck, and pancreatic cancers will serve a broader patient population beyond UroPartners' traditional urologic oncology base. This expanded scope is expected to generate additional patient volume from referring oncologists and multidisciplinary cancer care teams throughout the Service Area who currently lack local access to adaptive radiation therapy.

The radiation oncology field has undergone significant evolution in treatment standards since the Facility's existing LINAC was installed. The emergence of online adaptive radiation therapy (OART) represents a paradigm shift in how radiation is planned and delivered. The shift toward adaptive radiation therapy is reflected in evolving clinical guidelines and peer-reviewed literature demonstrating superior target coverage, and improved organ-at-risk sparing when treatment plans are adapted to daily anatomy. As noted in the Purpose of Project section, a retrospective study of prostate cancer patients treated with the Varian Ethos system found that adaptive plans achieved target coverage benchmarks in 418 out of 422 treatment fractions, significantly outperforming non-adaptive plans. These findings reflect a broader industry consensus that adaptive therapy represents the current standard for precision radiation oncology.

Further, advances in CT simulation technology have raised the standard for treatment planning accuracy. Modern simulation CT systems, such as the proposed SOMATOM go.Sim, incorporate AI-driven automated contouring and wider bore designs that improve patient positioning and workflow efficiency. These capabilities were not available when the Facility's current simulation equipment was acquired, and the gap between current equipment and contemporary standards continues to widen.

The Facility's existing equipment does not support adaptive radiation therapy workflows and cannot deliver the level of precision that current industry standards demand. Without this expansion, the Facility will be unable to offer care consistent with evolving best practices, placing its patients at a disadvantage relative to those with access to institutions that have adopted these technologies.

ATTACHMENT 31
77 Ill. Admin. Section 1110.270- Necessary Expansion (c)(2)

The proposed project represents a meaningful expansion in the scope of services available at the Facility. Currently, the Advanced Radiation Center of Chicago provides conventional external beam radiation therapy, primarily for prostate cancer and other urologic malignancies. The acquisition of the Varian Ethos system will expand the Facility's capabilities to include:

- Online adaptive radiation therapy (OART), which is not currently available at the Facility or, to the Applicants' knowledge, at any other freestanding radiation center within the 10-mile Service Area outside of downtown Chicago academic medical centers.
- Stereotactic body radiation therapy (SBRT) for renal cell carcinoma and other select indications, expanding treatment options for patients who are not surgical candidates.
- Expanded treatment of non-urologic malignancies, including breast, lung, pancreatic, gastrointestinal, gynecological, and head and neck cancers, using adaptive protocols that account for daily anatomical variability.
- Enhanced CT simulation capabilities through the SOMATOM go.Sim system, including AI-driven organ-at-risk contouring that accelerates treatment planning and supports the adaptive workflow.

This expansion of scope is driven by patient demand, referral patterns, and the recognition that patients within the Service Area currently lack convenient access to adaptive radiation therapy. By broadening the range of cancers treated and the sophistication of treatment delivery, the Facility will serve a larger and more diverse patient population while maintaining the specialized focus that distinguishes it from general hospital-based radiation oncology departments.

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 Varian Ethos linear accelerator (LINAC) and a SOMATOM go.Sim CT scanner are projected to achieve or exceed applicable target utilization levels within 12 months of installation. These projections are supported by documented patient demand, a well-established referral base, historical procedure volumes, and regional cancer incidence data.

Appendix B of the Health Facilities Planning Board's rules establishes target utilization levels for certain categories of major medical equipment. For linear accelerators, the applicable standard is 3,000 procedures in a hospital setting. There is no specific standard that exists for this equipment category in a non-hospital setting. For CT scanners used in radiation therapy simulation, the applicable standard is 3,600 procedures in a hospital setting. Appendix B does not include a specific benchmark for CT simulation equipment in a non-hospital setting.

The Advanced Radiation Center of Chicago currently serves a substantial patient population requiring radiation therapy services. In the most recent calendar year, the Facility delivered approximately 3,000 treatments using its existing LINAC. This volume reflects referrals generated through UroPartners' network of over 90 providers, as well as referrals from external oncologists and primary care physicians within the Service Area.

UroPartners referred approximately 3,000 patients in the most recent calendar year for procedures utilizing CT and linear accelerator equipment. With the acquisition of the proposed equipment, the Applicants project continuation of this volume without disruption in patient care, resulting in more than 3,000 procedures annually across both modalities. This projection is conservative, as the Facility anticipates additional volume growth from:

- Expanded scope of services, including adaptive radiation therapy for breast, lung, pancreatic, gastrointestinal, gynecological, and head and neck cancers, which will generate referrals from multidisciplinary oncology teams beyond UroPartners' existing urologic oncology base.
- Reduced treatment delivery times (approximately 15 minutes per session with the Varian Ethos system), which will increase effective daily throughput compared to the existing LINAC.
- Elimination of referrals to outside facilities for patients who currently require adaptive radiation therapy capabilities unavailable at the Facility.
- Faster turnaround times and improved access will encourage internal referrals and greater procedural efficiency.

The SOMATOM go.Sim CT system will be utilized primarily for radiation therapy simulation a required step for every patient beginning a new course of radiation treatment. As such, CT simulation volume is directly tied to LINAC patient volume. Each new patient requires at least one CT simulation scan prior to treatment initiation, and some patients require additional scans for re-simulation during their treatment course.

Based on the projected LINAC patient volume above, the CT scanner is expected to perform approximately 3,000 simulation scans in the first 12 months. Additional utilization will be generated by diagnostic CT imaging for urologic evaluation, including staging scans for newly diagnosed cancers, CT urography for hematuria evaluation, and surveillance imaging for patients in active monitoring protocols.

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

Regional cancer incidence data further support the projected utilization levels. According to the Illinois Department of Public Health, prostate cancer is the most commonly diagnosed non-skin cancer among men in Illinois, with approximately 10,000 new cases annually statewide. A substantial proportion of these patients are candidates for radiation therapy as a primary or adjuvant treatment modality. Kidney cancer, including clear cell renal cell carcinoma, accounts for more than 2,000 new cases annually in Illinois, with select patients eligible for stereotactic body radiation therapy. Breast cancer, lung cancer, and pancreatic cancer—all of which will be treated at the Facility using adaptive protocols represent additional significant sources of patient demand.

Given the Facility's location within the 10-mile Service Area, its established referral network, and the limited availability of adaptive radiation therapy in the northern suburban region, the Applicants are confident that the projected patient volumes are achievable and that both pieces of equipment will meet or exceed applicable utilization thresholds within 12 months of acquisition.

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 does not exceed the applicable capital expenditure minimum and qualifies as an equipment acquisition or service expansion not requiring demonstration of financial viability under this Section.

May 21, 2026

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

Re: Advanced Radiation Center of Chicago
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 Advanced Radiation Center of Chicago and Solaris Health Holdings, LLC, I, Justin Cohen, M.D., hereby attest that the project costs will be $8,629,000. Applicants will fund $7,705,000 of the project construction and equipment along with the necessary working capital and operating deficits with existing cash and securities. The balance of the project costs which equal $924,000 account for costs associated with the facility lease. 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,

Justin Cohen, M.D.
President
UroPartners, LLC

ATTACHMENT 36
Economic Feasibility
Projected Operating Costs and
Total Effect of the Project on Capital Costs

Pursuant to the Illinois Administrative Code Section 1120 Appendix A (a)(3), a project's cost must be at or below the RS Means for the new construction of a medical office building housing major medical equipment in excess of the Board's capital expenditure threshold. At the time of the application, the RS Means for new construction of Medical Office Building housing newly acquired major medical equipment in this area of the state is $981.69 per GSF. This project is slated to be completed in the third quarter of 2027, and the application RS Means is $981.69 per GSF. The proposed cost per GSF for this project is $590.85 and thus meet the Board's Criteria.

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 (LINAC and CT Scan)	$540.03	-	1,574	-	-	-	$850,000	-	$850,000
Contingency	$50.83	-	1,574	-	-	-	$80,000	-	$80,000
TOTALS	$590.85	-	1,574	-	-	-	$930,000	-	$930,000
* Include the percentage (%) of space for circulation									

Projected Operating Costs

The projected direct annual operating costs for the first full fiscal year at target utilization are $2,913,367.32, based on the fully allocated salaries, benefits, and supplies associated with operation of the proposed equipment and related service. Based on projected annual utilization of 6,000 procedures, consisting of 3,000 accelerator procedures and 3,000 CT scan procedures, the projected direct annual operating cost is **$485.56 per procedure / unit of service.**

Total Effect of the Project on Capital Costs

The total projected capital cost of the project is $8,629,000. Based on projected utilization of 6,000 procedures in the first full fiscal year at target utilization, **the total effect of the project on capital costs is $1,438.17 per procedure / unit of services $8,629,000**.

ATTACHMENT 37
Safety Net Impact Statement

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 the Advanced Radiation Center of Chicago will be an office-based lab clinical setting. The facility is not considered a healthcare facility as defined by the Illinois Health Facilities Planning Act (20 ILCS 3960). However, the Applicant do operate the UroPartners Surgery Center and are providing the charity care data for that facility below.

CHARITY CARE			
	2022	**2023**	**2024**
Net Patient Revenue	**$9,956,553**	**$4,238,821**	**$15,402,191**
Amount of Charity Care (charges)	$0	$0	$0
Cost of Charity Care	$0	$0	$0

ATTACHMENT 39
Flood Plain Requirements

May 21, 2026

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

Re: Advanced Radiation Center of Chicago - Flood Plain Requirements

Dear Mr. Kniery:

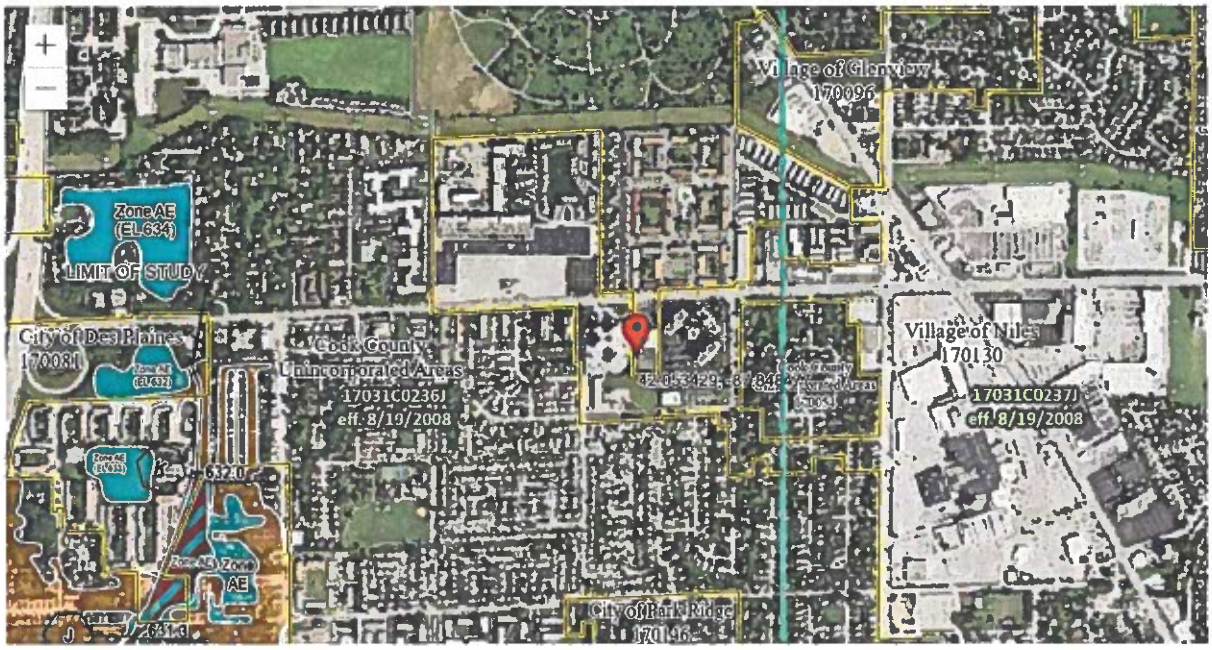
As representative of Advanced Radiation Center of Chicago, I, Justin Cohen, M.D., affirm that our proposed site complies with Illinois Executive Order #2005-5. The site located at 8915 West Golf Road, Niles, Illinois 60714 is not located in a flood plain, as evidence please find enclosed a map from the Federal Emergency Management Agency ("FEMA").

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

Sincerely,

Justin Cohen, M.D.
President
UroPartners, LLC

ATTACHMENT 39
Flood Plain Requirements



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

INDEX OF ATTACHMENTS