UNIVERSITY OF MEDICINE AND PHARMACY

"CAROL DAVILA", BUCUREȘTI

DOCTORAL SCHOOL

MEDICINE

ANATOMIC AND IMAGING CORRELATIONS OF THE PROSTATO-SEMINAL STRUCTURAL COMPLEX

PHD THESIS ABSTRACT

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CONTENTS OF THE DOCTORAL THESIS

Fundamental problem; hypothesis, objectives, research methodology

Hypothesis

Prostate disease is one of the most common and important health problems among middle-aged and older men. With the increasing prevalence of conditions such as benign prostatic hyperplasia and prostate cancer, the impact of these diseases on quality of life and the healthcare system is significant. Technological progress and advances in diagnosis and treatment have greatly improved the prognosis for patients, but challenges remain, particularly in the early detection and effective management of prostate diseases. In this context, a thorough understanding of prostate pathology and the implementation of effective prevention and treatment strategies are essential to reduce the morbidity and mortality associated with these conditions.

Detailed knowledge of prostate anatomy plays a crucial role in the diagnosis and treatment of prostate pathology. The prostate, a gland located below the bladder and surrounding the urethra, has a complex structure composed of different areas that can be distinctly affected by different conditions. For example, benign prostatic hyperplasia mainly affects the transition zone of the gland, while prostate cancer frequently occurs in the periphery. Accurate understanding of these anatomical aspects allows doctors to perform diagnostic procedures, such as biopsies and magnetic resonance imaging (MRI), with greater accuracy, and to plan surgery or non-surgical treatments in an optimized way.

A thorough knowledge of prostate anatomy is also essential for managing complications and side effects of treatments. Procedures such as radical prostatectomy, radiotherapy and brachytherapy require extreme precision to minimize the risks of urinary incontinence and erectile dysfunction, common complications due to the prostate's proximity to critical anatomical structures such as the urinary sphincter and erectile nerves.

Thus, a comprehensive approach to prostate pathology, based on a solid understanding of the anatomy of this gland, is essential to improve clinical outcomes and quality of life of patients. In the era of modern medicine, continuing education and research in prostate pathology remains fundamental to the development of innovative and effective therapeutic strategies.

The personal motivation for doing a PhD on prostate pathology stems from the desire to make a significant contribution to the understanding and treatment of prostate disorders, given the major

impact these diseases have on men's health and quality of life, as well as from a passion for research and innovation in the medical field.

As a radiologist I understood since the first year of residency the importance of anatomy in the daily medical practice of an imaging physician, helping to increase the quality of the medical act of diagnosis or treatment. I believe that a good radiologist is also a good anatomist, having the ability to more easily project in space the anatomical elements and the relationships between them.

Objectives

My objectives for this paper are the following:

1. To perform a detailed dissection of the prostate gland and adjacent sympathetic structures, highlighting the topographic relationships between the prostatic plexus, pelvic sympathetic chains, hypogastric plexuses and urogenital elements involved in urinary continence and sexual function.
2. Morphological characterization of the prostatic plexus and how sympathetic fibers distribute in the prostatic capsule, bladder neck and prostatic urethra in order to better understand the anatomical implications in oncologic surgery and minimally invasive prostate therapy.
3. Correlation of anatomical findings with the location of lesions visualized by prostatic MRI, in order to understand the nerve tracts affected by tumor enlargement and possible functional consequences.
4. Evaluation of the accuracy of biparametric MRI in the diagnosis and staging of prostate cancer in relation to histologically confirmed pathology, in the context of the urological patient's diagnostic pathway.
5. Determining the role of magnetic resonance imaging in the management algorithm of the prostate cancer patient, both in the initial diagnostic phase and in treatment planning (targeted biopsies, surgery, focal therapy).
6. To identify the advantages and limitations of MRI sequences used in the evaluation of prostatic lesions, with emphasis on the ability to differentiate between benign and malignant lesions and the impact on clinical decisions.
7. Proposing an anatomic-radiologic synthesis, based on dissection and imaging data, to serve as a guide for urologic or radiologic interventions with risk of sympathetic plexus involvement.

Research methodology

My study is par excellence a descriptive study starting from a broad briefing on the current state of knowledge about prostate anatomy. The most important data collected on the current state of knowledge are to be found in the extensive presentations in the general part. We realized after this information effort that there is a significant information deficit on the detailed anatomy of the sympathetic nervous system.

My study is based on the dissection of formolized cadavers in the anatomy laboratory. These are adult cadavers as well as embryonic and pediatric cadavers.

We used eight adult cadavers between 60 and 80 years of age and four female cadavers, two three months old and two four months old. The handling of cadavers was done according to the law no. 104/27.03.2003, which regulates the use of cadavers in anatomy laboratories in Romania.

Formolization of the cadavers was performed by injecting three liters of 9% formalin solution into the femoral artery and then immersing the cadavers in a formalin bath of the same concentration for 60 days. After formalinization, the cadavers underwent a toiletting process.

Dissections were done in planned stages according to the surgical dissection in the plans. Basically, most of the time, I studied the surgical protocols for access in my areas of interest. This helped me in more objectively establishing anatomic-clinical correlations.

We used complex surgical kits as well as surgical dissection loupes. For two cadavers, we performed both sagittal and transverse sections of the pelvis.

The dissection fields were photographed with a NIKON D7500 digital camera under special illumination with four photographic lamps with light filters.

Even in these professional studio conditions, getting perfect details was often very difficult. I think it is not without interest that for each image presented in the thesis there are at least twenty images of the same subject in the database.

The resulting photographs were processed with specialized software, Adobe Lightroom and Adobe Photoshop, without interfering in any way with the scientific data. Image labeling was done with Adobe Illustrator.

Study I: Evidence by dissection of the formation of the prevertebral aortic sympathetic plexus and its relationships

1. Introduction

Pelvic dissection is one of the most difficult dissections in anatomy. The proximity of the pelvic floor makes the approach to the organs of interest extremely difficult. Sections through the pelvis in different planes are required. I have not set out to do a complete review of pelvic anatomy, but from my clinical experience, I have identified certain structures that I felt it would be useful to focus on in particular.

In the clinic, the most common interest in vesico-prostate-seminal structures is in the border region between the bladder and the prostate, in the area called the interdeferential trigon(1).

Knowledge of the relationships of the posterior aspect of the prostate, prostate base, seminal vesicles and vas deferens is the touchstone in efforts to establish a correct imaging diagnosis.

The situation of the bulbourethral glands will be dealt with separately.

2. Materials and methods

In the laboratory of the Anatomy Discipline of the University of Medicine and Pharmacy "Carol Davila" in Bucharest, we performed dissections on ten male cadavers and one 3-month-old fetal cadaver (amsculin sex). The cadavers were previously formolized by injecting a 9% formalin solution into the femoral artery, followed by a 30-day preservation period in tanks with the same formalin solution. The conditions for the handling of cadavers provided for by Law 104/2003 were fully respected.

Dissections were performed in a staged, anatomic-planar fashion using both anterior and posterior approaches to the pelvic region. Special attention was given to the vesico-prostate-seminal region, following the relationship between the bladder, prostate, seminal vesicles, vas deferens, pelvic fascia and adjacent vasculo-nervous structures.

Serial sections were made through the prostate to reveal the seminal colliculus, the course of the ejaculatory ducts and the disposition of the prostate glands. The bulbourethral glands were also dissected in situ and analyzed in the context of their relationships with neighboring structures.

The dissection specimens were documented photographically and the images were digitally edited - exclusively for clarity - without altering the scientific content. The resulting observations were compared and discussed in the context of the literature.

3. Results

The results of the pelvic pelvic dissection performed in this study provide a detailed and nuanced perspective on the anatomic vesico-prostate-seminal relationships, with direct implications for clinical and imaging practice.

A first essential aspect is the close relationship between the **posterior aspect of the prostate and the fundus of the Douglas sac**, where the anatomical elements - seminal vesicles, vas deferens and prostatico-seminal vessels - are arranged in a compact and functionally interdependent manner. These observations support the idea that this region is difficult to explore and interpret imagistically, and clear delineation between components is often impossible(2).

Figure 1: Postero-superior view of the bottom of the Douglas bag (red arrow)

1. Duct deferent; 2. Seminal vesicles; 3. Prostate - posterior face; 4. Perirectal fascia; 5. Rect.

Dissection confirmed **fusion of the connective tissues at the base of the prostate**, making it impossible to clearly identify the junction between the seminal vesicles and vas deferens. This fusion may be relevant for the morphologic explanation of local invasion in prostatic neoplasia and justifies the difficulties encountered in interpreting MRI images in this region. We also observed that the **pelvic parietal fascia has a protective role over the cavernous nerves**, which have a strictly subfascial course in the paraprostatic portion. This morphologic detail anatomically validates *nerve-sparing* prostatectomy techniques, which attempt to preserve erectile function by maintaining the integrity of the fascia(3).

Figure 2: Presentation of the pelvi-prostatic fascial system showing the vascular relationships The figure shows the parietal fascia (1), and deep to it the cavernous nerve pathway can be identified (2). The parietal fascia continues directly with the prostatic fascia (3).

Regarding the anterior region of the prostate, this remains **one of the least explored areas**, and our dissection revealed relevant aspects: the vesico-prostatic venous plexus does not have the classic reticulated appearance described in atlases, but consists of a complex of anastomosed venous ectatia, difficult to control intraoperatively. This finding explains the **significant bleeding** observed in classical digital enucleation, in which hemostasis can only be achieved by compression and not by ligation or cauterization.

Figure 3: Detail image visualizing the behavior of the dorsal penile vein at the level of the vesico-prostatic junction.

Another important element is the **prostatic capsule**, whose characteristics - sub-millimeter thickness, firm adherence to the parenchyma and lack of a cleavage plane with respect to it - make it a relative barrier to tumor progression. These data support clinical observations of early extracapsular invasion in prostatic adenocarcinoma(4).

Figure 4: Detail image showing the central dissection of the prostatic capsule in intimate contact with the prostatic parenchyma.

On inseriate sections, it was possible to trace the **disposition of the ejaculatory ducts**, which approach well before opening into the seminal colliculus. They are surrounded by vascularized connective tissue, with an almost cavernous appearance, suggesting a possible functional role in maintaining seminal fluid continence. **The seminal colliculus**, in the middle third of the prostate, appears well defined as a distinct protuberance flanked by prostatic sinuses - an observation rarely described in detail in the literature.

Figure 5. Cross-section of the prostate to show the seminal colic (1), the urethra (2) and the ejaculatory ducts in the vicinity of the urethra (3,4).

As far as **the bulbourethral glands** are concerned, our in situ dissection represents, to the best of our knowledge, an original contribution. These glands have been identified in the thickness of the transverse perineal muscle, in an intramuscular position functionally justified by the mechanism of secretion evacuation into the urethra by muscle contraction. This observation reinforces the hypothesis of an active muscular control of the secretion of the bulbourethral glands.

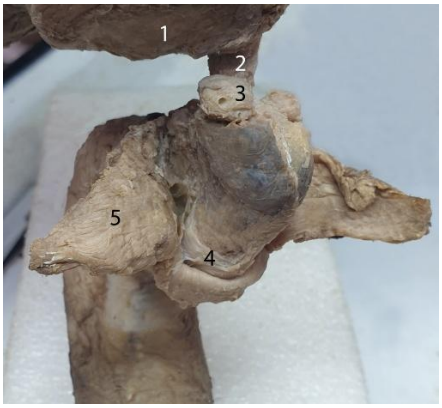


Figure 6: Dissection of the prostato-penile complex where we can visualize in the upper part of the image the lower edge of the prostate (1) from which the embryogenic urethra (2) starts, posterior and slightly inferior to it, the left bulbourethral gland (3). In order to visualize the bulbourethral glands, it was necessary to dissect at the base of the penis, where the albuginea is visualized (4)

Lastly, the structure of **the seminal vesicles**, with their bulbous appearance and hemispherical lumen, supports the accumulation and sedimentation of seminal fluid, explaining the predisposition to stone formation. The vascularization of this region, derived from vesical branches

derived from the prostatic vascular trunk, is complex and may be a weak point for tumor dissemination through continuity solutions in the seminal wall(5,6).

Figure 6: Dissection specimen of the vesiculo-prostatic complex, postero-lateral view showing the vas deferens (1), seminal vesicles (2) and the posterior aspect of the prostate (3)

4. Discuss

My study, carried out through detailed dissections of the male pelvic region, highlights the structural complexity of the vesico-prostate-seminal apparatus and reveals a number of important observations that may contribute to a deeper understanding of the topography of this area, with direct implications for clinical, imaging and oncologic practice.

1. **The difficulty in dissecting the deferento-seminal junction** confirms the fused nature of the connective tissues at the base of the prostate. This anatomical aspect, rarely described in the literature, explains the difficulties encountered in establishing precise tissue boundaries in surgery or in pelvic imaging interpretation.
2. **The continuation of the pelvic parietal fascia with the prostatic visceral fascia** at the contact with the posterior aspect of the prostate emphasizes the fascial continuity and its importance as a surgical and oncologic plane. This fascia plays a protective role over vasculo-nervous elements and also becomes a key area for tumor invasion.
3. **The path of nerves and vessels to the prostate**, which perforate the parietal fascia and penetrate into the space between the fascia and the capsule, accounts for the anatomical mechanism of local tumor dissemination. This pathway of fascial penetration, particularly in the 'prostatic horns', explains the early onset of periprostatic metastases in locally advanced cancers.

4. **The close relationship between the cavernous nerve and the pelvic parietal fascia** supports the idea that preserving this fascia during surgery (*nerve-sparing* prostatectomies) can significantly contribute to the preservation of postoperative erectile function.
5. **The venous structures anterior to the prostate** are represented by anastomosed ectatia, which communicate with both the penile veins and the periprostatic veins draining into the internal iliac system. This organization, which differs from the classical atlas representations, explains the hemorrhagic risk of previous surgery and justifies the difficulty in achieving effective hemostasis - the only effective method being compression.
6. **The prostatic capsule**, sub-millimeter thick and intimately adherent to the parenchyma, proves to be only a relative barrier to tumor invasion. The lack of a real plane of dissection between the capsule and glandular tissue makes "clean" surgical excision difficult in capsulopenetrating tumors, and extracapsular invasion must be understood in this morphologic context.

5. Conclusions

In conclusion, these observations not only complement existing information from the literature but provide a solid morphologic basis for radiologic interpretation and intraoperative decisions. The pelvic dissection performed in this study contributes to a more precise mapping of the vesico-prostate-seminal region and provides further arguments for understanding tumor dissemination, technical difficulties in pelvic surgery and the functional mechanisms involved.

Study II: THE ROLE OF MRI IMAGING IN PROSTATE CANCER

1. Introduction

Prostate cancer is the fourth most common form of malignancy globally, surpassed by lung, breast and colorectal cancers, according to the International Agency for Research on Cancer (IARC) through the Global Cancer Observatory in 2022. In men, it ranks second in frequency after colorectal cancer.

Prostate cancer is the eighth leading cause of cancer mortality in both sexes and all age groups (after lung, colorectal, liver, breast, gastric, pancreatic, esophageal, and esophageal cancers) and ranks fifth as the leading cause of cancer death in male patients (after lung, liver, colorectal, and

gastric cancers) (7). According to the Cancer Statistics Center of the American Cancer Society, prostate cancer is expected to be the second most common malignancy after breast cancer by 2024. It will also be the fifth leading cause of cancer mortality in the general population, ahead of lung and bronchus, colorectal, pancreatic, breast and lung cancers. In the male population, prostate cancer is estimated to be the second leading cause of cancer mortality, after lung and bronchial cancers(8). There are certain characteristics associated with an increased risk of prostate cancer, such as advanced age, race (particularly patients of African origin) and first-degree family history of the same diagnosis. Other risk factors include obesity, the BRCA2 gene mutation, and rarer factors such as Lynch syndrome(9).

Given the increasing frequency of prostate cancer and its potentially severe progression, it is essential to develop an effective strategy aimed at early detection and appropriate management of this malignancy in order to reduce its impact on both the population and the health care system(9).

2. Materials and methods

We conducted a retrospective study by reviewing our institution's oncology database from January 2016 to November 2023, and included 50 male patients, aged between 50 and 84 years, who underwent MRI examinations using a 1.5 T magnetic field machine.

Confirmation of the diagnosis of prostate cancer in suspicious lesions identified by imaging was performed by histopathologic examination of fragments obtained by:

- radical prostatectomy (in most cases),
- ultrasound-guided transrectal prostate biopsy,
- and, to a lesser extent, from fragments obtained during transurethral resection of the prostate (TURP).

Prostate biopsy was used in patients who were not eligible for radical prostatectomy, divided into three categories:

1. Patients with locally advanced disease in whom negative surgical margins could not be obtained.
2. Patients with pelvic adenopathy or distant metastases in whom it was necessary to confirm the prostatic origin of the primary tumor.

3. Patients with multiple comorbidities in whom the risks of radical prostatectomy were considered too high.

TURP-derived fragments have been used in a small number of cases, mainly in patients with advanced central gland cancer, in whom TURP was performed as a palliative measure to relieve urinary symptoms.

No patients were excluded from the study.

According to institutional regulations, retrospective studies of this type do not require prior approval by the ethics committee.

Clinical, pathological and imaging parameters were collected from electronic medical records and the data were centralized in a Microsoft Excel© file.

3. Results

On T2-weighted images, prostatic cancer lesions appeared hyposintense in 46 of the 50 cases (92%), isosintense in one patient (2%) and moderately hypersintense in 3 patients (6%), all of which were greater than 8 mm in diameter. These data support the high accuracy of T2 sequences in detecting lesions suspicious for prostatic neoplasia.

Diffusion restriction on DWI sequences and ADC maps was present in 43 cases (86%), indicating slightly lower accuracy compared to T2-weighted images, but still diagnostically significant.

On T1-weighted images, the tumor lesions were in 94% of cases (47 patients) isosemmal and in 6% of cases (3 patients) moderately hypersemmal, also in the context of lesions with a diameter greater than 8 mm. These results confirm that T1-weighted imaging is not reliable in the evaluation of suspicious prostatic lesions.

	Hyposemnal	Isosemnal	Hyperseminal
T1	0 (0%)	48 (96%)	2 (4%)
T2	46 (92%)	1 (2%)	3 (6%)
DWI	2 (4%)	5(10%)	43 (86%)
ADC	45 (90%)	5(10%)	0 (0%)

Table 1. MRI appearance of prostatic lesions on T1-weighted, T2-weighted, DWI and ADC maps

4. Discuss

In our study, we aimed to evaluate the accuracy of biparametric magnetic resonance imaging (bpMRI) in the diagnosis of prostate cancer, in order to assess the degree of agreement between the results obtained and those reported in the literature.

In order to correctly characterize suspicious lesions of the prostate gland on MRI, it is essential to have a good knowledge of prostate anatomy and pathology, the specific imaging appearance of prostate adenocarcinoma, and the patient's management after diagnosis, in order to be able to recognize normal and pathological changes that may occur after treatment.

In this context, our study evaluated the MRI appearance of prostatic adenocarcinoma on T2-weighted images, DWI sequences and ADC maps in a group of 50 patients. The results showed a high accuracy of T2-weighted sequences, which allowed to raise the suspicion of prostate cancer in all analyzed cases.

T1-weighted images are of limited usefulness in the evaluation of prostatic parenchymal parenchyma, but they allow accurate recognition of post-biopsy bleeding. It is important to note that hemorrhage may be more extensive than the puncture needle track because prostate cells produce citrate, a substance with anticoagulant properties. The blood may mimic or mask the tumor, which is why MRI is recommended 6-8 weeks after the biopsy, as bleeding persists after this period in only a small number of cases.

In addition to these considerations, T1-weighted imaging is valuable in the evaluation of regional adenopathies and bone metastases, thus contributing to the correct staging of the disease(10,11).

T2-weighted (T2WI) sequences highlight both anatomical aspects and morphological features of the prostate gland, as well as its relationships with neighboring structures(12).

Due to the increased density of glandular and ductal tissue, together with the high water content, the normal peripheral zone of the prostate appears homogeneously hyperintense on T2-weighted

images(10,12). The transition zone shows a mixed, heterogeneous signal intensity on T2-weighted images, due to the increased cell density caused by epithelial and stromal hyperplasia, characteristic of benign prostatic hypertrophy, which generates the appearance known as "organized chaos". Due to its rich fibrous tissue content, the central area has low intensity on T2-weighted images, as does the pseudocapsule surrounding the gland. The histologic features of prostate cancer are directly reflected in its imaging appearance. Due to the dense aggregation of malignant cells and low water content, prostatic adenocarcinoma appears hypointense on T2-weighted images, and the lower the intensity, the higher the tumor aggressiveness(10).

Regarding the transition zone, there are certain imaging criteria that should raise the suspicion of prostate cancer on T2-weighted images, even in the absence of correlation on DWI sequences and ADC maps. These include:

- invasive behavior ("organized chaos disruption"),
- dark edges,
- lenticular or spindle-shaped,
- A homogeneous, intermediate to low focal signal, known as the "faded charcoal pattern"(12,13).

Since not every abnormality detected on T2-weighted images is equivalent to prostate cancer, it is important to consider other pathologies that may mimic malignancy, such as acute, chronic or granulomatous prostatitis, post-biopsy hemorrhage, effects of irradiation, scarring, atrophy or effects of hormonal therapy(10,12).

In terms of changes seen on MRI, prostatitis can occur:

- hypointense on T2-weighted images,
- with low signal on the ADC map,
- and contrast-enhanced dynamic contrast-enhanced imaging (DCEI). However, it usually has a banded, wedge-shaped or diffuse distribution, in contrast to prostate cancer, which appears as round, oval or irregular lesions with significantly lower ADC values(12,13).

In addition to assessing the appearance of the prostate gland and any suspicious nodules, the length of the membranous urethra should be noted, as it is a positive predictor of urinary continence at 3 and 6 months after prostatectomy(14).

Diffusion Diffusion Imaging (DWI) reveals the movement of water molecules within both benign and malignant prostate tissue. In prostate cancer, characterized by increased cellularity within an extensive glandular epithelium, water molecules cannot move freely(10,12).

When the DWI is performed with different values of the magnetic gradient (varying b-values), the apparent diffusion coefficient (ADC) map can be obtained.
Low ADC values indicate areas with reduced movement of water molecules, i.e. tumor areas(10).

When evaluating prostate tissue, the association of DWI images with the ADC map is essential: Hypointense areas on ADC and hypointense areas on DWI suggest a malignant process(10).

It has been shown that the ADC value is inversely proportional to the Gleason score, so the lower the ADC values, the higher the tumor grade, making DWI the most important functional imaging technique(10,12).

However, DWI has certain limitations:

- In some cases, benign prostatic hyperplasia may have diffusion restriction, mimicking malignancy.
- Also, DWI is susceptible to artifacts, generated by bowel peristalsis, the presence of rectal gas or the presence of hip prostheses(12).

In our study, the appearance of lesions on DWI and ADC map, although considered to be of high accuracy in identifying malignant lesions, was found to be less accurate compared to T2-weighted images. Correlation of DWI/ADC sequences with T2-weighted images, however, resulted in the highest accuracy in prostate cancer detection.

Pesapane et al. state that in their study based on the use of bpMRI, no cases of high-grade cancer were missed, which was also confirmed in our study(15).

High-grade tumors, including those with Gleason score ≥ 8 and those with extraprostatic extension, were efficiently identified by correlating DWI/ADC images with T2-weighted images.

As emphasized by Palumbo et al., T2-weighted and DWI images, together with the ADC map, are sufficient not only for prostate cancer detection, but also for the assessment of tumor aggressiveness(10,16).

Dynamic contrast-enhanced imaging (DCEI) consists of obtaining T1-weighted images after intravenous administration of gadolinium-based contrast agents. Intense and early contrast uptake is strongly suggestive of prostate cancer, but it should be noted that prostatitis and hyperplastic nodules may show a similar uptake pattern(10).

However, DCEI significantly alters the imaging diagnosis in a small number of cases, which is why, in recent guidelines, its role is considered limited in the evaluation of prostate cancer. Therefore, DCEI is used only when the quality of T2WI and DWI images is inadequate, or when diagnostic uncertainties persist after evaluation of these sequences, especially in suspicious peripheral tumors. In contrast, the role of DCEI in transition zone assessment is minimal(10,13,15,17).

Although the origin of prostate cancer in the central zone is rare, it may be affected by the extension of tumors in peripheral or transitional zones. In these cases, even if T2WI, DWI and ADC map images do not show abnormalities, DCEI may show early focal contrast uptake(13).

The DCEI also provides valuable information on local recurrence in patients who have undergone radical prostatectomy, focal therapy or transurethral resection, in the setting of altered zonal anatomy(10,12,13).

After external beam radiotherapy, both DCEI and DWI can be useful in the detection of recurrence, with superior performance to T2WI(14). Compared to DWI, DCEI is also useful after brachytherapy, as radioactive seeds can generate significant artifacts on DWI(14).

Using magnetic resonance spectroscopy (MRSI), citrate and choline levels can be determined. Thus, prostate cancer can be suspected in areas with abnormal metabolic expression. Currently,

MRSI has a limited role in the routine evaluation of prostate cancer and is mainly used in research(10).

Currently, multiparametric MRI (mpMRI) includes:

- T1- and T2-weighted images,
- Diffusion Diffusion Imaging (DWI),
- and dynamic contrast contrast-enhanced imaging (DCEI), while biparametric MRI (bpMRI) includes only:
- T2-weighted images
- and DWI(15,18).

Because some studies show that the detection rate of clinically significant prostate cancer is similar between mpMRI and bpMRI, in our daily practice, in patients with elevated PSA, we prefer the use of the latter(15).

The advantages of bpMRI over mpMRI include:

- similar rate of clinically significant cancer detection,
- lower false positive rate,
- low cost,
- short acquisition time (less than 15 minutes),
- reduced interpretation time,
- and the absence of risks associated with gadolinium-based contrast agents such as:
    - venous catheterization,
    - side effects,
    - nephrogenic systemic fibrosis,
    - gadolinium retention
    - and its deposition in the brain parenchyma or other tissues(15,17-19).

The risk associated with the use of gadolinium-based contrast agents exists even in patients with normal renal function, especially in the context of repeated MRI examinations(15).

However, the importance of the DCEI should not be underestimated as it can be used when:

- DWI cannot be properly assessed due to poor signal-to-noise ratio or presence of artifacts(13,18),
- or in already treated patients in whom local recurrence is suspected(18).

To optimize the use of MRI in the management of patients with prostate cancer, the Prostate Imaging Reporting and Data System (PI-RADS) provides information and recommendations on the role of each sequence and when it should be used, the latest version being PI-RADS v2.1(13).

Song et al. state that the diagnostic performance of bpMRI applying the PI-RADS v2.1 criteria is lower compared to mpMRI, but high enough to consider bpMRI a viable screening tool for the detection of clinically significant prostate cancer(20).

In our study, the use of PI-RADS v2.1 applied on bpMRI helped us to estimate the likelihood of clinically significant prostate cancer and to identify all clinically relevant cases.

The role of Magnetic Resonance Imaging (MRI) in the assessment of prostate cancer extension, local and distant metastases

After raising the suspicion of prostate cancer based on MRI, it is essential to evaluate tumor extension. Extraprostatic extension is suggested on MRI when observed:

- loss of rectoprostatic angle,
- irregular margins and protruding outline of the gland,
- asymmetry of neurovascular bundles
- their direct involvement(9).

The asymmetry of the gland itself should not be interpreted as suspicious, as it frequently occurs in benign prostatic hyperplasia(15).

In the seminal vesicles, invasion is suggested in case of abnormally low T2 signal, diffusion restriction or contrast uptake in these structures(10).

Extraprostatic extension, invasion of neurovascular bundles and seminal vesicles, large tumor size, presence of lymph node metastases and positive surgical margins are all signs of locally advanced disease and are associated with increased risk of local recurrence(21).

Even an anatomic feature, such as the absence of prostatic pseudocapsule at the apex, has been correlated with local recurrence of the disease(21).

For evaluation of distant metastases, especially bone metastases, several studies recommend its use:

- whole-body MRI with DWI sequences,
- bone scintigraphy,
- computerized tomography (CT) scan
- PET/CT(9).

Some studies support that when evaluating lymph node or bone metastases by MRI, the use of dynamic contrast-enhanced imaging (DCEI) is useful and should be included in the examination protocol(9,10).

Prostate cancer treatment and post-therapy evaluation

Treatment is customized according to cancer extension and preoperative risk stratification, including options such as:

- active surveillance,
- focal therapy (including cryotherapy and high intensity ultrasound - HIFU),
- radical prostatectomy,
- radiotherapy (both brachytherapy and external radiotherapy),
- hormone-blocking therapy (antiandrogens and luteinizing hormone-releasing hormone - LHRH),
- chemotherapy.

For tumors located in the prostate gland, the preferred therapeutic methods are:

- radical prostatectomy,
- radiotherapy, possibly in combination with hormone therapy(9,21)

In terms of recurrent disease, certain surgeries - particularly those that preserve the neurovascular bundles and urethral sphincter - are associated with a higher risk of local recurrence.

Pelvic recurrence may also manifest as lymph node or bone metastases, which emphasizes the importance of regular monitoring of patients treated for prostate cancer to allow early intervention in the early stages of recurrence.

In most cases, due to the small size of the recurrent tumor tissue, neither digital rectal curettage nor imaging methods are able to show the disease with certainty, making it difficult to guide a biopsy.

Early detection of recurrence allows the use of:

- surgical treatment,
- radiotherapy
- cryoablation for local recurrences, whereas distant metastases require systemic therapy(21,22).

5. Conclusions

The main limitation of our study was the fact that all included patients were referred to our institution for imaging examinations already having a high suspicion of prostate cancer based on clinical (symptoms, digital rectal cough) and biochemical (elevated PSA values) criteria. Thus, working with an experienced clinician who correctly identifies patients with a high probability of prostate malignancy could influence the interpretation of the MRI, increasing the risk of confirmation bias.

In this context, the radiologist may be tempted to classify suspicious or indeterminate lesions as malignant, even if the MRI appearance of some of them would have been compatible with alternative diagnoses such as acute or chronic prostatitis.

To properly assess the overall effectiveness of bpMRI, a larger group of patients, including:

- prostate cancer patients,
- patients with benign prostate pathologies,
- patients without obvious clinical or biochemical signs.

Also, in order to eliminate bias in imaging interpretation, the radiologist should not have information about the clinical suspicion or the estimated percentage of malignant cases, which would allow an objective assessment of indeterminate lesions, taking into account both benign and malignant diagnoses.

Study III: VARIABILITY OF PROSTATE VASCULARIZATION AND ITS IMPACT ON PERCULTANEOUS EMBOLIZATIONS

1. Introduction

Benign prostatic hyperplasia (BPH) is a common pathology in the male population over 50 years of age, with an incidence of approximately 50%, and is associated with lower urinary tract symptoms (LUTS) that considerably affect quality of life. Therapeutic options for BPH include drug treatment, surgical interventions (transurethral incision of the prostate - TUIP and transurethral resection of the prostate - TURP), as well as minimally invasive methods such as prostatic artery embolization (PAE) and prostatic urethral lift(23).

I aimed in this study to evaluate prostatic artery embolization as a minimally invasive method of treatment for BPH, a procedure that consists of superselective embolization of the prostatic arteries (PA) with the aim of reducing the volume of the prostatic parenchymal volume and improving the symptomatology of patients. First described as a treatment for BPH in 2010 by Carnevale, this procedure has subsequently been adapted and developed by numerous interventional radiology centers(24).

2. Materials and methods

This retrospective study was based on DSA examinations performed in 35 male patients, aged between 50 and 83 years, diagnosed with benign prostatic hyperplasia (BPH) and undergoing the prostatic artery embolization (PAE) procedure. The procedures were performed between March

2021 and May 2023 by two interventional radiologists in the Endovascular Network Department. All patients agreed to participate in the study by signing the preprocedural informed consent form.

In our department, we used the left brachial approach for PAE, with a 5F introducer (Terumo™), 5F JR-shaped catheter (125 cm) from Merit Medical™, Radiofocus™ metal guidewire 0.035"' (180 cm) from Terumo™ and Omnipaque™ 350 mgI/ml neionic contrast agent (GE Healthcare™). For superselective catheterization of the prostatic arteries, we used the Direxion Transend 14™ preloaded torqueable microcatheter from Boston Scientific™.

3. Results

We were able to identify the origin of the prostatic artery (PA) in all patients included in the study. The most common origin was in the internal pudendal artery (IPA) in 37.1% of the 70 hemipelvises analyzed, followed by the anterior gluteal trunk above the bifurcation (27.1%), superior vesical artery (21.4%) and obturator artery (11.4%). Rarer origins were identified in the inferior gluteal artery, in 2.8% of cases. Compared with other studies, the percentages of each origin vary slightly, but the main order of frequency is maintained(25-27).

The data obtained in my study were compared with previously published results by other relevant authors in the field of prostatic artery embolization (Table 2). The percentage distribution of prostatic artery origin in the present study is consistent with the literature, although there are notable variations between the different series analyzed.

Table 2. Comparison of prostatic artery (PA) origin with other studies in the literature

Study	**IPA (%)**	**Anterior gluteal trunk (%)**	**Superior vesical artery (SVA) (%)**	**Occluding artery (%)**	**Inferior gluteal artery (IGA) (%)**
Serbănoiu et al.	26 (37,1%)	19 (27,1%)	15 (21,4%)	8 (11,4%)	2 (2,8%)
Bilhim (2010)	28 (56%)	14 (28%)	-	6 (12%)	2 (4%)
Bilhim (2012)	73 (34%)	38 (17,8%)	42 (20%)	27 (12,6%)	8 (3,7%)

Study	IPA (%)	Anterior gluteal trunk (%)	Superior vesical artery (SVA) (%)	Occluding artery (%)	Inferior gluteal artery (IGA) (%)
Zhang (2015)	32 (27,9%)	45 (39,5%)	37 (32,6%)	-	-
De Assis (2015)	45 (31,1%)	-	43 (28,7%)	28 (18,8%)	-
Monaco	8 (17,4%)	26 (56,6%)	-	2 (4,3%)	-

Although the percentages vary slightly from one study to another, a common general trend in the predominant origin of the prostatic artery is maintained. In my study, the internal pudendal artery (IPA) was the most common source, followed by the anterior gluteal trunk and superior vesical artery - a pattern that confirms the importance of tailoring the angiographic technique to these anatomic variants.

Origin of the prostatic artery

Prostatic artery originating from the internal pudendal artery

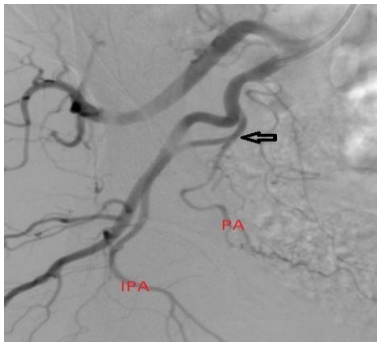


Figure 1. The case of a patient in whom the origin of the prostatic artery (indicated by the arrow) is located at the level of the internal pudendal artery (IPA), without significant angulations at the origin and without significant collaterals.

We can consider this example as an "ideal patient" for PA catheterization in terms of vascular anatomy. However, it is essential to follow all steps of the procedure and to carefully check the catheterized artery before embolization.

Prostatic artery originating in the anterior gluteal trunk

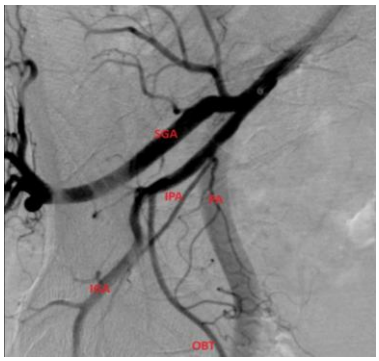


Figure 2. Prostatic artery (PA) originating from the anterior gluteal trunk. The obturator obturator tract (OBT) and internal pudendal artery (IPA) can be identified as branches originating from the same anterior trunk. Following the origin of the PA, fine arterial branches corresponding to the inferior bladder arteries are observed.

The prostatic artery origin at this level is usually accessible for catheterization due to the shape of the JR catheter, which can be positioned close to the PA origin, thus providing adequate support and optimal control for handling the Direxion microcatheter.

Origin of the prostatic artery in the superior vesical artery

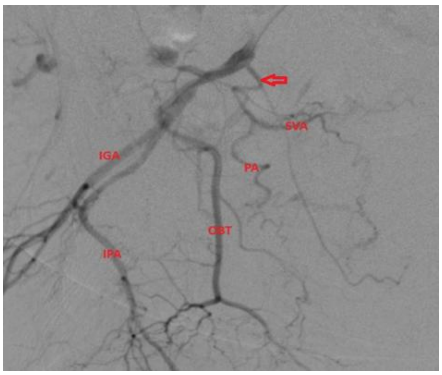


Figure 3. The case of a prostatic artery (PA) originating from the superior vesical artery (SVA), indicated by the arrow. The PA originates from the proximal portion of the SVA. In this anatomic variant, it is essential to position the microcatheter distal to the origin of the PA to avoid non-directed bladder embolization.

Prostatic artery with distal origin at the level of the internal rurus artery

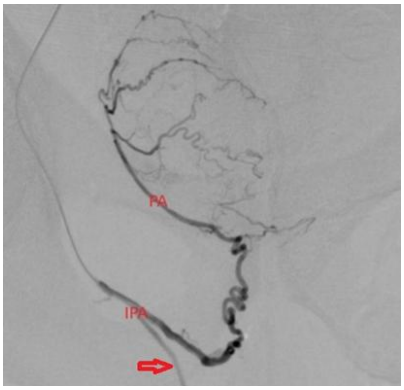


Figure 4. This picture shows a particular case in which the prostatic artery (PA) originates distally from the internal pudendal artery (IPA) with an ascending trajectory. The key issue in this case is to perform a superselective catheterization to avoid accidental embolization of the penile artery (indicated by the arrow).

The importance of superselective catheterization in prostatic artery with common trunk or anastomosis

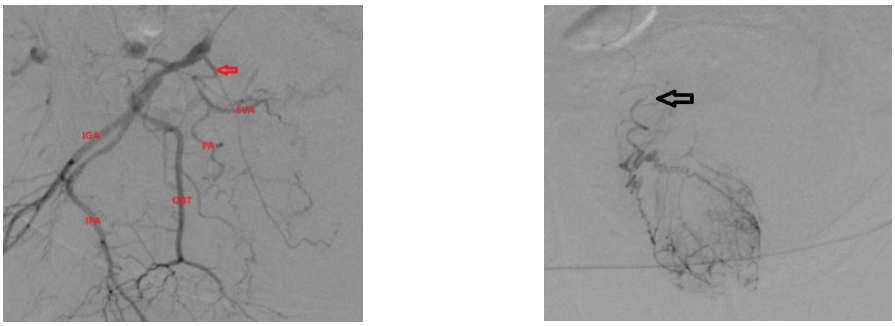
In situations in which the prostatic artery (PA) has a common trunk with other arterial branches or is in a network of anastomoses, superselective catheterization becomes an essential step of the procedure. I aimed to pay particular attention to these cases, as an embolization performed proximally, before the bifurcation of arteries or near an anastomosis, may lead to non-directed embolization of untargeted structures such as bladder, rectum or penis.

By performing a superselective catheterization, we aimed not only to maximize the efficiency of prostatic embolization, but also to minimize the risks associated with ischemia of adjacent tissues. This principle becomes particularly important in anatomic variants in which the PA shares its origin with the inferior vesical artery, the middle rectal artery or the penile artery.

Following this step allows a precise embolization, focused exclusively on the prostate parenchyma, thus ensuring a superior safety profile and better patient recovery.

We can frequently identify prostate arteries (PA) that share a common trunk with the superior or inferior bladder artery. In such cases, it is necessary to position the microcatheter distal to the

origin of the bladder arteries to ensure a targeted embolization and prevent damage to the bladder vasculature.

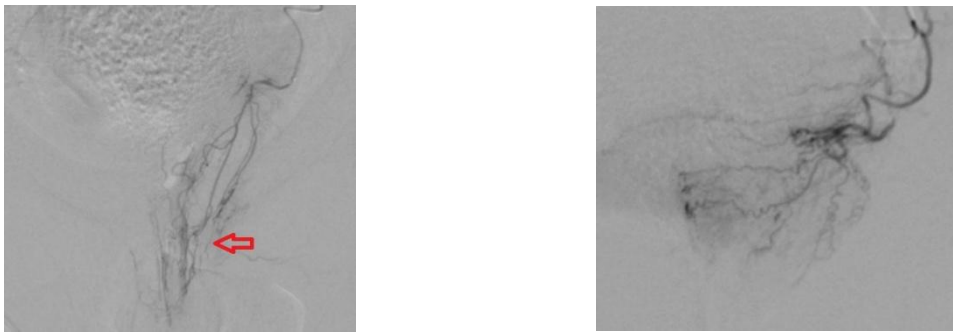


(**a**) (**b**)

Figure 5. (a) The origin of the prostatic artery (PA) from the superior vesical artery (SVA), indicated by the arrow; (b) Correct positioning of the microcatheter (arrow) distal to the origin of the PA, necessary to ensure a targeted embolization of the prostate, evidenced by the characteristic 'blush' appearance on contrast opacification.

In the case of arterial anastomoses and collateral circulation, it is essential to follow the same rule of distal microcatheter positioning in order to achieve a correctly directed embolization. Otherwise, the embolization particles may end up in unwanted territories, causing small areas of necrosis.

Middle rectal artery originating from the prostatic artery



(a) **(b)**

Figure 6. (a) Cases are encountered in which the middle rectal artery originates from the posterior branch of the prostatic artery (PA). The characteristic vertical blush of the rectal arteries can be seen, an important landmark for identification (arrow); (b) Correct positioning of the microcatheter in the anterior branch of the PA is necessary to achieve targeted embolization and avoid rectal tissue injury(28). Correct positioning should always be demonstrated before embolization by a DSA acquisition showing the characteristic prostatic blush.

Post-procedural complications

No major periprocedural events, such as non-directed embolization with necrotic areas in the rectum, bladder or penis, were recorded in any of the patients included in the study. Also, none of the patients experienced post-procedural vascular complications such as pseudoaneurysms or arterial dissection.

Minor post-procedural side effects were pelvic pain within the first 24 hours, reported in 22 of the 35 patients included in the study (62.8%).

4. Discuss

As the procedure of prostatic artery embolization (PAE) has become increasingly popular in recent years, I considered it important to present in this paper the method used and the challenges encountered in relation to the anatomic variability of the prostatic artery origin. Although the male pelvic arterial vasculature exhibits significant variability, certain patterns repeat and can be used as a benchmark. Compared with the current literature, the results of my study highlight some percentage differences in PA origin, but the same order of the three most common origins: superior vesical artery (SVA), internal pudendal artery (IPA), and anterior gluteal truncus anterior commonus is maintained. This information may help to improve the technique, especially in terms of reducing radiation exposure to the patient and the physician.

EAP is a demanding procedure, and its success depends directly on the skills and knowledge of the interventional physician. For this reason, I consider it essential to highlight some useful practical information. The left brachial approach, with the use of a 5F introducer, has been shown to be an effective option, facilitating catheterization of both hemipelvises and being associated with a lower incidence of local postprocedural complications.

The five-step arterial mapping method, applied prior to embolization, was an organized approach for PA identification with a significant impact on reducing procedural time and radiation exposure. By correlating these steps with the results obtained in the study, we were able to localize the prostatic artery based on the most common anatomical origins, confirming the usefulness of the method by the similarity of the results with those reported in other reference studies.

An important element in identifying the PA is its characteristic corkscrew appearance, which helps to differentiate it from other small-caliber pelvic vessels.

After performing superselective catheterization of the PA, I recommend the use of 200-300 μm embolizing particles, appropriately diluted with contrast and saline, injected slowly. Repeated check with DSA acquisitions is necessary to prevent reflux of embolizing particles from the PA into other arterial branches.

Technical challenges may arise during the procedure, such as the emergence angle of the AP or the presence of highly variable trajectories and branches, which can be difficult for early stage interventional radiologists. The solution is to shape the metal guidewire at a similar angle to the trajectory of the artery to facilitate navigation and catheterization.

Given that benign prostatic hyperplasia is one of the most common pathologies in elderly men, it is to be expected that atherosclerotic changes - such as stenoses and vascular tortuosities - are also encountered in EAP procedures, complicating catheterization and increasing the duration of the procedure and radiation exposure. In these cases, the correct positioning of the JR catheter is essential, providing optimal support for the microcatheter to cross the atherosclerotic plaques.

It is mandatory to identify the collaterals or anastomoses of the prostatic artery before embolization in order to take the necessary measures for a correctly targeted embolization. The most common collaterals involve the middle rectal artery, inferior bladder arteries and internal pudendal artery. In cases in which superselective catheterization is not possible, embolization of the respective branch with micro-coils is recommended to ensure an effective outcome(29).

The endovascular navigation technique described in this paper is also applicable in other specialized procedures designed to treat rare postsurgical complications such as bleeding or

pseudoaneurysms. Cases with excellent results and low morbidity have been reported(30,31). Tailoring the embolic material (coil, adhesive, particles) to the affected branch of the internal iliac artery is essential.

All aspects discussed must be taken into account when performing embolization to ensure an efficient, safe and effective procedure without post-procedural complications.

5. Conclusions

Prostatic artery embolization (PAE) is a safe and effective method for the treatment of lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH), as long as the technical principles are followed and the anatomical variability of the pelvic arterial vasculature is known. Due to its minimally invasiveness and low complication rate, the popularity of this procedure has increased significantly in recent years.

Compared with other studies, we observed percentage differences in the origin of the prostatic artery, but all papers converge on the same three common variants. It is essential for early-career interventional radiologists to be aware of all possible origins of PA in order to be able to perform catheterization correctly and to provide patients with BPH with effective and safe treatment.

Performing targeted embolization is one of the essential steps in the success of the procedure, contributing significantly to reducing the risk of post-procedural complications(32).

Conclusions and personal contributions

For study number 1, "Dissection study of the prostate, seminal vesicles and bulbourethral glands for the purpose of highlighting and topography of the elements":

The conclusions are:

The present study highlighted the morphologic complexity of the vesico-prostate-seminal region and allowed a detailed reconstruction of the local anatomic relationships by careful pelvic dissection. The results obtained confirm that this area involves a tight and interdependent tissue organization, often difficult to interpret imagistically or to approach surgically.

Dissection proved:

- the dense connective tissue at the base of the prostate gland, which is difficult to separate clearly by classic anatomical methods;
- pelvic fascial continuity, with protective role on cavernous nerves and direct implications in nerve-sparing surgery;
- the presence of an atypical vesico-prostatic venous plexus, consisting of anastomosed venous ectatic anastomoses, with increased intra-operative hemorrhagic risk;
- how the prostatic capsule represents a relative anatomical barrier to tumor progression, without a real cleavage plane to the parenchyma;
- the positioning of the ejaculatory ducts and the potential functional role of the pericanalicular connective tissue in maintaining seminal fluid content;
- the intramuscular localization of the bulbourethral glands, justified by the need to empty the contents into the urethra by contraction of the perineal transverse perineal muscle.

These observations provide a solid morphologic basis for understanding tumor dissemination, pelvic surgical difficulties, and accurate interpretation of high-resolution imaging explorations.

Personal contributions are:

Through this study, I aimed to investigate in detail the anatomy of the vesico-prostate-seminal region, starting from the practical difficulties encountered in its clinical, imaging and surgical evaluation. My personal contributions include:

- performing original and thorough dissections on ten male cadavers with multiple approaches (anterior and posterior);
- Systematic photographic documentation of each dissective stage and clear highlighting of loco-regional relationships;
- a detailed description of the bulbourethral glands in situ, an aspect rarely documented in the literature and realized in this study;
- identification of the subfascial course of the cavernous nerve and its correlation with surgical implications related to the preservation of erectile function;
- analyzing the structure of the seminal colliculus and ejaculatory ducts on serial sections, hypothesizing the functional role of pericanalicular tissues;
- anatomical correlation of the periprostatic venous plexus with intraoperative hemorrhagic risk, proposing new interpretations of the pelvic vasculature;
- formulation of original morphological interpretations of tumor dissemination in prostate and seminal vesicle cancers, based on the fascial course and vascular layout revealed by dissection.

For study number 2, "The role of MRI imaging in prostate cancer":

The conclusions are:

- The study confirmed the usefulness of biparametric magnetic resonance imaging (bpMRI) in the evaluation of patients with suspected prostate cancer, supporting the integration of this method into the modern diagnostic algorithm.
- T2-weighted sequences showed the best accuracy in identifying suspicious lesions, being superior to T1 images and comparable with DWI/ADC.
- Correlation of T2WI images with DWI and ADC maps significantly increased diagnostic accuracy, especially for clinically significant tumors (Gleason score ≥ 7).
- The study demonstrated bpMRI's ability to differentiate between benign and malignant lesions and its potential to reduce unnecessary biopsies.
- MRI evaluation also contributed to local staging of the disease by identifying extraprostatic extension, seminal vesicle invasion and bone metastases.

- BpMRI has proven to be a viable alternative to mpMRI, with additional benefits in terms of cost, examination time, avoidance of gadolinium-related risks and patient acceptability.
- The results support the use of bpMRI not only as a diagnostic tool, but also as a means of therapeutic guidance and tumor recurrence monitoring.

Personal contributions are:

- In this retrospective study, we aimed not only to validate the literature, but also to apply biparametric imaging in a real clinical setting, demonstrating its relevance and effectiveness.
- We systematically identified imaging features of suspicious prostatic lesions, correlating T2 hyposignal with diffusion restriction on DWI and decreased ADC values, which are essential for tumor risk stratification.
- We emphasized the importance of integrated interpretation of T2WI and DWI images, demonstrating their superiority in clinically significant cancer detection compared to T1 images or even DCEI sequences.
- We documented with specific examples the inversely proportional relationship between ADC value and Gleason score, suggesting the predictive value of this parameter for tumor aggressiveness.
- We contributed to the recognition of imaging signs of extraprostatic extension, vesicular invasion and tumor recurrence, which are essential for treatment planning.
- We reviewed the technical and logistical advantages of bpMRI, making the case for its current use over mpMRI in resource-limited centers.
- We assessed the limitations of the study and proposed to extend the research to more diverse populations, including patients without clinical suspicion, in order to reduce confirmation bias and objectively validate the method.

For study number 3, "Variability of prostate vascularization and its impact in percutaneous embolization":

The conclusions are:

- Prostatic artery embolization (PAE) is a minimally invasive, safe and effective therapeutic method for the relief of lower urinary tract symptoms (LUTS) caused by benign prostatic hyperplasia (BPH), offering comparable results to TURP, but with a lower rate of complications.
- The technical and clinical success of EAP depends directly on a thorough knowledge of the pelvic anatomy, in particular the origin and course of the prostatic artery, as well as the correct identification of collaterals and anastomoses.
- In this study, the most common origins of the prostatic artery were: internal pudendal artery (37.1%), anterior gluteal trunk (27.1%) and superior vesical artery (21.4%), results that are in agreement with the literature.
- The application of the five-step method for arterial mapping has proven useful in efficiently localizing the prostatic artery, helping to reduce procedure time and limit radiation exposure.
- Superselective catheterization, followed by careful embolization of the anterior branches of the prostatic artery, was essential to avoid complications such as rectal, penile or bladder ischemia.
- There were no major post-procedural complications and minor side effects (pelvic pain) were transient and manageable.
- The data obtained support the need to individualize the technical approach according to the patient's anatomy, with particular attention to the collaterals and common branches of the prostatic artery.

Personal contributions are:

- In this study, I aimed to provide a practical and applicable perspective for early career interventional radiologists by detailing the essential steps for safe and effective prostatic artery catheterization.
- We have implemented and validated a five-step arterial mapping method, which allowed a systematic and reproducible approach to identify the prostatic artery and perform superselective embolization.

- We documented with images and detailed descriptions the anatomic variability of PA origin and emphasized the importance of common trunks and anastomoses in embolization planning, which are essential to prevent complications.
- We demonstrated the efficacy of the left brachial approach and the advantages of using a JR + torqueable microcatheter system for bilateral pelvic catheterization, reducing the incidence of local complications.
- We integrated notions of dissectional and angiographic anatomy, providing a clear correlation between anatomical observations and the applied interventional technique.
- By comparative analysis with the international literature, we confirmed the internal pudendal artery as the main source of PA and provided concrete data on other important variants of origin, useful in guiding clinical decisions.

I believe that this work represents not only a personal contribution to the detailed understanding of the PAE technique, but also a valuable didactic tool for the training of young specialists in interventional radiology.

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