Is it possible a non-invasive tool of diagnostic and prognostic of the prostate cancer by Imaging assessment?

Poster No.: C-0594
Congress: ECR 2011
Type: Scientific Exhibit
Authors: A. C. Georgescu¹, R. Berisha², A. Bondari², S. Bondari², A. Manda², M. E. Andrei²; ¹Craiova, Dolj/RO, ²Craiova/RO
Keywords: Genital / Reproductive system male, Pelvis, Ultrasound-Power Doppler, MR, CT, Diagnostic procedure, Imaging sequences, Neoplasia, Hyperplasia / Hypertrophy, Inflammation
DOI: 10.1594/ecr2011/C-0594

Any information contained in this pdf file is automatically generated from digital material submitted to EPOS by third parties in the form of scientific presentations. References to any names, marks, products, or services of third parties or hypertext links to third-party sites or information are provided solely as a convenience to you and do not in any way constitute or imply ECR's endorsement, sponsorship or recommendation of the third party, information, product or service. ECR is not responsible for the content of these pages and does not make any representations regarding the content or accuracy of material in this file.

As per copyright regulations, any unauthorised use of the material or parts thereof as well as commercial reproduction or multiple distribution by any traditional or electronically based reproduction/publication method ist strictly prohibited.

You agree to defend, indemnify, and hold ECR harmless from and against any and all claims, damages, costs, and expenses, including attorneys' fees, arising from or related to your use of these pages.

Please note: Links to movies, ppt slideshows and any other multimedia files are not available in the pdf version of presentations.

www.myESR.org
Purpose

Introduction

Compared with most cancers, cancer of the prostate (CaP) tends to grow slowly. In contrast to breast cancer, the present consensus is that imaging has no role in screening for CaP and most clinicians recommend Imaging exams only for staging of this cancer. However, there are important applications of Ultrasonography (US) and, increasingly, Magnetic Resonance Imaging (MRI) and dynamic multidetector computed tomography (CT) in the prostate.

It is estimated approximately 20% of USA men will have clinical CaP during their lives, yet as many as 46% of men older than 50 years have at least microscopic cancer in their prostate glands. Because the morbidity of treatment may outweigh its benefits, in Europe it is common not to treat asymptomatic men for CaP if they are older than 70 years. The problem is many elder men develop benignant prostatic hyperplasia (prostate adenoma), which is symptomatic and after a conservative surgery the pathologic report presents the CaP as an incidentaloma, which is partial removed and necessitates complete treatment.

In general, CaP survival rates will depend on:

- The stage of the disease
- The patient's age and general health
- Whether the cancer has just been diagnosed or has come back (recurred)
- The Gleason score and the level of PSA.

The stages of CaP play a role in the survival rates. 5-year relative CaP survival rates are recognised:

- 100 percent for localized or regional disease,
- 33.3 percent for distant stage (metastases),
- 79.5 percent for unstaged.

Classical screening and diagnosis of CaP

The chief tool for CaP screening is the serum concentration of prostate specific antigen (PSA). However, PSA is not specific for cancer: as many as 80% of the men with an elevated serum PSA concentration do not have CaP.

A lesser role is played by digital rectal examination (DRE), which has a low sensibility (40% of the CaP arise in the anterior peripheral zone, 20% in the transitional zone and 10% in the central prostate zone, which can not be examined by the urologist finger).
To integrate multiple factors for the prediction of an initial biopsy outcome, image-based clinical support models were implemented, and the performance of a support vector machine (SVM) was considered superior to the performance of an artificial neural network (ANN) or a multiple logistic model [1]. But this model is not available for all and the future will decide his popularity.

When these examinations present important abnormalities, the next step is usually represented by the "blind" biopsy with a systematic 10 or more core samples for the detection of the CaP. However, there are cases with not proved cancer (in 70%-75% cases), and so how many biopsies should we perform to a patient and what frequency/what interval should they be performed? There is not a reasonable consensus.

The reasons for an imaging screening and diagnosis of CaP

The goal of the management of CaP is an as earlier as possible diagnostic, with a non-invasive technique, repeatable, available for all and with a low cost.

The particular anatomy of the prostate and of the seminal vesicles offers large possibilities to the imaging techniques of diagnosis. Indeed, the prostate is structured in two parts:

A- Glandular portion (2/3):

- lateral lobes - make most of pass of prostate, located lateral to urethra;
- posterior - behind urethra, below ejaculatory ducts (CLINICAL NOTE - this is the only palpable prostate region via DRE);
- medial - around urethra;

B- Fibromuscular portion (1/3): anterior lobe - anterior to urethra, no glandular substance.

The lateral lobes and the posterior glandular lobe are well demarcated in hyper signal T2WI and STIR, while the medial and the anterior portions are distinct in iso/hypo signal T2WI and STIR; that results we must not underestimate the prostate volume in T2 acquisitions by neglecting the peripheral zone, in iso-signal with the periprostatic fatty tissue. In native T1WI and CT acquisitions the whole gland is more or less homogeneous (Fig.1 on page 5). Moreover, the peripheral gland enhances much more than the central periurethral zone. The seminal vesicles have the same comportment as the peripheral prostatic gland (Fig. 2 on page 5). The prostatic capsule is smooth and well demarcated in T2WI; the periprostatic vasculature is salient outside the capsule, merged to the vesical-prostatic inferior pedicle into the recto-vesical ligament (Fig. 3,4,5,6,7,8,9). There are anatomical variants of the prostate in asymptomatic men or related to the infertility (Fig. 10,11).
Anatomically, the prostate is supplied from the internal iliac arteries by the prostatico-vesical arteries [2; 3]. The prostatico-vesical artery gives rise to two terminal branches, the prostate artery and the inferior vesical artery. The prostate artery then divides into urethral and capsular arteries. The latter divides into two sets on the surface of the gland, one located anteriorly and the other posterolaterally. Centripetal branches from these vessels perforate the capsule to supply the prostatic parenchyma as they course towards the periurethral zone.

As one might intuitively expect, it has been shown pathologically that neovascularity/microvessel density in prostate carcinoma is an independent predictor of pathologic stage and it has a presumably malignant potential [4]. Some recent observations suggest that the vasculature could play a more central role in the regulation of the normal prostate and prostate tumors; therefore, the factors controlling blood flow, endothelial cell proliferation, and other aspects of angiogenesis in the normal prostate and in prostate cancers are almost unknown.

Vascular density and vascular invasion correlates significantly with capsular perforation, seminal vesicle invasion, positive margins of resection, perineural invasion, high grade, and pathological stage, as demonstrated a study of van den Ouden and col [5]. In their experience, multivariate analysis showed that vascular invasion was associated with a 2.5-fold increased risk for clinical progression, 2.3 for biochemical progression, and 2.7 for cancer-specific survival.

Moreover, many studies indicate that the vasculature could be regulated, directly or indirectly, by androgens, and castration-induced involution is a therapeutical method of choice for CaP. In addition, the growth of a human prostate cancer cell line (PC3) in nude mice is clearly inhibited after treatment with the angiogenesis inhibitor angiostatin [6].

**Purpose**

Imaging flow assessment may become even more important in the preoperative non-invasive diagnostic and treatment of CaP; our purpose is to illustrate and present an analysis of the new vasculature features of CaP on Doppler US, multidetector enhanced CT and MRI of these patients, and to make the differential diagnosis with non-malignant prostate pathology and non-prostatic pelvine malignancy using the imaging techniques.
Images for this section:

**Fig. 0:** Axial and coronal T2WI (A, B), coronal STIR (C, F) and axial and coronal T1WI (D, E): the peripheral glandular area is well differentiated from the periurethral (central) part in T2 and STIR acquisitions.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
**Fig. 0:** Axial and coronal T2WI (A, B), axial and coronal T1WI (D, E) and axial and coronal STIR (C, F): the seminal vesicles are usual symmetrical and well visualized in hypersignal T2 and isosignal T1.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
**Fig. 0:** Coronal T2WI visualizes symmetrical vesical-prostatic vascular plexus.
**Fig. 0:** Axial T2WI visualizes symmetrical vesical-prostatic vascular plexus and the vesical-prostatic ligament.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
Fig. 0: Coronal STIR useful for the symmetrical vesical-prostatic vascular plexus.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
**Fig. 0**: Parasagittal T2WI visualizes the vesical-prostatic vascular plexus.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
Fig. 0: 3D and MIP techniques are useful for analyze of the symmetry and of the peripheral vasculature of the prostate and of the seminal vesicles.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
**Fig. 0:** The same 3D reconstruction is visualized in a different projection (coronal view).

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO

**Fig. 0:** 3D reconstruction from STIR acquisitions illustrates the seminal vesicles, useful for the clinicians imaging understanding and for analyze of the symmetry.
**Fig. 0:** BI, 57-year-old: The anatomy of a large prostate in axial T2WI (a), sagittal T2WI (b, c), axial T1WI Fat-Sat with contrast (d), sagittal T1WI with contrast (e) and coronal T2 of the seminal vesicles (f). Note the enlarged peripheral glandular area with secretor/ fluid signal in all acquisitions.
**Fig. 0:** BMG, 50-year-old: Malformation with prostate and seminal vesicles hypoplasia and a piriforme bladder visualized in sagittal T2WI (a, b) and coronal STIR images (c, d), as compared with the full developed seminal vesicles and prostate in similar planes of acquisition (sagittal T2WI-e, coronal T2WI-f).

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
Methods and Materials

We performed a prospective study between June 2008 and November 2010 of the prostate vasculature as it was demonstrated on Doppler US in 61 consecutive patients (range 28-78 years); among them 25 performed MRI exam and/or multislice CT. The inclusion criteria for the US as first imaging exam were relevant clinical symptoms and abnormal findings on digital rectal examination (DRE). Patients with increased level of the PSA over 4ng/ml, proven CaP or with suspect lesion on US were included in the sublot that underwent further imaging exams. The local ethics committee approved the study protocol and an informed consent of the all patients was provided.

**The protocol of US examination included:**

- Detection of a suspect prostatic mass: a hypoechoic mass with/without calcifications, usually localized in the outer area of the prostate (peripheral zone and central zone), with/without capsular invasion and with salient new vasculature (Fig. 1 on page 17);

- Determination of the gland volume with TRUS/transabdomino-pelvic measurements:

  \[ \text{Gland Volume} = \text{width (w) x height (h) x length (l) x 0.5} \]

- Determination of the expected tumor volume:

  \[ \text{Predicted PSA} = \text{gland volume x 0.12} \]

  This is useful to calculate the

  \[ \text{Excess PSA} = \text{serum PSA - predicted PSA} \]

  and then to evaluate the

  \[ \text{Expected tumor volume} = \frac{\text{excess PSA}}{2} \]

  based on the formula: 1 cm$^3$ of cancer produces near 2 ng/ml of PSA.

- Determination of the average tumor dimension:

  \[ \text{Tumor volume} = \frac{(w + h + l)}{3}. \]

  In the cases we used Aloka US equipments the prostate volume, the tumor volume, and the predicted PSA were automatically calculated (Fig. 2 on page 17).

- Determination of the abnormal prostate vasculature on color/power Doppler and spectral Doppler. The cases were classified upon a qualitative characterization: absent/low-symmetrical vasculature for normal prostate, abnormal asymmetrical increased
vasculature, suspect for malignancy, and abnormal diffuse hyper vasculature in benign cases (Fig. 3, 4). Spectral Doppler confirmed the arterial and venous flow-type and allowed the differential diagnosis with the twinkling artifacts that may be present in prostate calcifications (Fig. 5,6). We calculated the mean pulsatility index (PI) and the mean resistive index (RI) values for the capsular artery when it was detectable.

**The standard protocol of MRI exam (1.5-T MRI system) included:** axial and coronal T1 and T2WI, axial/coronial acquisitions with fat saturation and 3D reconstructions for the estimation of the symmetry and volume of the prostate and of the seminal vesicles, axial and coronal T1WI with contrast agents (Gadovist from Bayer Schering Pharma, MultiHance® from Bracco Diagnostics, Inc.). Sagittal acquisitions are less important in the assessment of the vesico-prostatic vasculature, but are usually included in the protocol for the determination of the local rapport.

**The multidetector CT exam** included native abdominal-pelvic scan and post contrast acquisitions in the arterial and venous phase, 2.5-5mm slice thickness, with multi planar reconstructions; CT was used in the evaluation of the stage of the disease and with special focus on the bony density, the pelvic and abdominal lymph nodes, the kidneys and the lungs. In the pelvis CT exam evaluated the prostate vasculature, the periprostatic fatty tissues, the vesical wall and the seminal vesicles appearance.
Fig. 0: Salient left periprostatic vasculature is more significant than the abnormal hypoechoic lesion in the center of the right lobe of the prostate.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
**Fig. 0:** Automatic determination of the prostate volume and of the PSA.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
**Fig. 0:** Duplex color and spectral Doppler present an arterial flow with low velocity indices suggesting new prostatic vasculature or hyperemia.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
**Fig. 0:** Duplex color and spectral Doppler present a venous flow in the anterior-superior prostatic capsule, without the possibility of diagnostic by DRE.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
Fig. 0: There is a Doppler signal of the urinary jet at the right ureteral ostium and of a twinkling artifact of a right lobe calcification.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
**Fig. 0:** The same case, with spectral Doppler useful as differential diagnosis.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
Results

Among all 61 patients examined on US, 25 presented clinical, biological and/or US abnormal findings and underwent further imaging exams; among them 21 were finally diagnosed with prostate cancer. Another 3 patients with abnormal Doppler US findings were biopsied without other imaging examination and malignancy was proved in 2 cases. The PPV of Doppler US was 82%.

The most important findings for CaP on US were considered the abnormal/asymmetrical increasing vascularity in number and velocity (Fig. 1,2), the low velocity indices of the prostate capsular arteries (RI less 0.70, PI less 1.50), the asymmetrical prostate enlargement, the unequal enlargement of the seminal vesicles, and the predicted value of PSA over 4 ng/ml (Fig. 3 on page 29).

Less specificity for CaP resulted for the hypo echogeneicity of the prostatic lesions and for the prostatic volume, which was more important in the periurethral hyperplasia (adenoma) (Fig. 4,5).

The transrectal US was not always possible, conditioned by the patient, local conditions or recent previous biopsies, but the most recent US machines are able to detect and calculate the desired parameters on the transabdominal US scans.

The MRI findings in 22 patients confirmed the abnormal US aspects and further targeted biopsies/ surgical biopsies confirmed the malignancy in 18 cases. In 3 cases with imaging abnormal findings and high PSA level, negative biopsies were considered false-negative results, because of the location of the abnormal imaging findings in the anterior-lateral prostatic area, no accessible to the DRE and difficult to biopsy (Fig. 6,7,8,9,10). The PPV of the MRI was 95%. The most important findings were considered for MRI exam the asymmetrical peripheral area in hyposinal with increasing signal intensity after contrast administration, new/enlarged vasculature with/without high velocities (proved by the presence of the void-signal in all acquisitions) located periprostatic and inside the suspect area of the gland, the asymmetrical prostate enlargement, the unequal enlargement of the seminal vesicles, the presence of lymph nodes enlargement and eventually the bony signal abnormality. The infiltration of the periprostatic fatty tissue or of the vesical / rectal walls is not significant in the early stages, and for the advanced stages the bony involvement occured in almost all cases.

Three cases of CaP suspected by US exam were further examined only by CT because of the suspicion of metastases. CT was not used for the early stages/ detection of the CaP, except 4 cases with post-intravenous contrast dynamic acquisitions for scientific reason,
in completion to the US and MRI acquisition (Fig. 11 on page 37). The detection of the prostate new vascularity was depending of the type of the multidetector CT, which allows fine slides and better reconstructions and was not significantly influenced by the iodinated contrast agent type.

As follow-up exam, CT was useful in the detection of local recurrence, capsular perforation, seminal vesicle invasion, vesical wall invasion, pelvic lymph nodes involvement, and lung and bony metastases (Fig. 12, 13, 14, 15, 16, 17, 18, 19, 20). US was useful for the detection of local recurrence, lymph nodes involvement, lung peripheral metastases or presence of an interstitial syndrome by mediastinal lymph nodes blockage, upon the Lichtenstein criteria (Fig. 21 on page 47) [7, 8]. In pelvis, MRI and CT were useful in the differential diagnosis of the extensive CaP from the trigonal vesical cancer (Fig. 22, 23, 24) and from the rectal cancer extensive to the prostate (Fig. 25, 26, 27).

**Discussion:**

Last decade the imaging techniques of diagnosis improved their performances, so there are already a lot of papers presenting the achievements of the US, MRI and spiral CT.

**Prostate Ultrasonography**

It is agreed early detection and early intervention of progressive CaP may help to reduce the 30,000 prostate cancer-related deaths each year [9]. Therefore not all CaP need treatment, some men may have so-called "latent" or "insignificant" tumors, thus precise ultrasound evaluation with proper biopsy will provide us with valuable information to make a decision between watchful waiting and appropriate early intervention.

The combination of prostate specific antigen (PSA) testing with transrectal ultrasound (TRUS) with subsequent ultrasound guided biopsies (random biopsy) and digital rectal examination (DRE) has been responsible for diagnosing most prostate cancers (PC) in the USA last years. In practice, a serum PSA > 3ng/ml, a PSA increase of 1ng/ml in a year, or abnormal DRE are the indications for TRUS [10]. Unfortunately, TRUS has several deficiencies. Only tumors in the peripheral zone can be detected reliably. Although 60% to 70% of CaP lesions are hypoechoic, most of the remainder are isoechoic and thus invisible by TRUS.

**Doppler and tissue harmonic imaging US**

Doppler characterization with/without contrast agents and Tissue Harmonic Imaging (THI) seems to improve the sensibility and specificity of US. Usually, cancer tissue shows a higher blood flow (tumor neovascularity) than that of normal tissue, so Doppler characterization improves detection and actual tumor size measurement. Harmonic technology improves spatial resolution and contrast resolution to discern very subtle
differences in grayscale, so the detection of the small hypoechoic masses is easier. Because the hypoechoic texture is not specific for prostate cancer, the Doppler signal is an alarm that indicates the biopsy or the Sono-elastography. The mean pulsatility index value for the capsular artery of group with CaP (1.49 ± 0.57) was significantly lower than that of benign control group (1.71 ± 0.52; \( P = .048 \)) according to study published in 2007 [11].

Some authors consider pathologic categories were not separable by apparent vascular measurement, because all pathologic categories showed low, moderate, or high vascularity; thus focal hyper vascular hypoechoic areas did not increase the likelihood of cancer in their study [11]. However, Mitterberger et al. have reported comparative data on the effectiveness of biopsies guided by transrectal, contrast-enhanced, color Doppler ultrasound (CECD-US) as compared to a systematic biopsy in 1,776 men between 2002 and 2006. They concluded the 5-core CECD-US-guided biopsy identified prostate cancer in 476/1,776 patients (27%), while the 10-core systematic biopsy identified prostate cancer in 410/1,776 patients (23%). The reducing on half of the biopsies samples with better accuracy is significant for the vascular characterization of the prostate cancer, with double detection rate using CECD-US targeted biopsy (10.8%) against systematic biopsy (5.1%) [13].

A prospective study published in 2008 presented improved statistical parameters of color Doppler versus grayscale sonography: sensitivity 88.23 vs. 73.52, specificity 66.66 vs. 33.33, positive predictive value 93.75 vs. 85.18, and negative predictive value 50 vs. 22.22, respectively [14].

The Full Prostate Ultrasonography concept

The future prostate US will add the Sono-Elastography or Real-Time Elastography (RTE) as a more sensitive method to detect the stiffness abnormalities, and combined with Doppler characterization we will realize the Full Ultrasonography (FU) for the prostate, a new concept already in use for the breast examination [15]. In addition, Doppler and RTE are able to detect the extracapsular spread, thus the tumor staging is improved. The aim of the FU is to use good ultrasound evaluation with guided staging (strategic) biopsy and eliminate the "guesstimations" from random biopsies [9]. In a study of Aigner and col, RTE targeted biopsy allows prostate cancer detection in men with prostate specific antigen 1.25 ng/ml or greater and 4 ng/ml or less with a decreased number of cores compared with that of systematic biopsy, with positive cancer cores of 24% in RTE targeted cores as compared with 5.1% in systematic cores [16]. It would be wrong practice if we will expect some amazing results from the RTE as a unique examination, because this technique is just complementary to the Doppler US. We should avoid the overestimation of any method, thus the score 4 or 5 Ueno/Tsukuba on RTE [17], suggesting malignancy, must be correlated with the presence of a new vasculature on Doppler for a positive diagnosis, otherwise a hard tissue with benign calcification could be misdiagnosed for malignancy on RTE, while the low vasculature suggests chronic prostatitis.
Localization of the tumor in the outer gland in over 60-80% cases is suspected when there is an excess PSA greater 2 ng/ml and it is easily to visualize on US because this region is more homogeneous; the cancer is present usually in the areas of anatomic weakness (entry of neurovascular bundle branches, seminal vesicles, and apex), with high risk for extracapsular spreading.

The anatomic weakness of the inner gland, the anterior apex and the bladder neck, are suspected when the excess PSA is 4 to 6 ng/ml and no lesion is found in the outer gland. TRUS sensitivity is less for the inner gland, but Doppler may be useful and FU is expected to be more accurate.

**Prostate MRI**

CaP enhances more rapidly and to a greater degree than normal tissue during the first pass on fast dynamic imaging. Moreover, poorly differentiated tumors show the fastest enhancement (Fig. 28,29,30,31). A wide range of accuracy figures can be found in the literature, from 54% to 90%. With the use of appropriate parameters, however, MRI can be expected to be superior to digital rectal examination in detecting extracapsular extension. MR spectroscopy may be helpful both for local staging and for noninvasive determination of the aggressiveness of a CaP. Typically, stimulated echo acquisition mode (STEAM) or point-resolved spatial selection (PRESS) is used with three-dimensional phase encoding (chemical shift imaging). The data can be fused with anatomic images. Because of their higher rate of cell proliferation and their greater cellular density, CaPs have higher than normal concentrations of choline. Also, the amount of citrate is lower than in normal tissue [18].

**Prostate Computed Tomography**

Despite the low accuracy of the CT in the early diagnosis of the CaP, we observed that the arterial phase is useful in the visualization of the vezical-prostatic arteries and their branches that are enlarged as compared with the opposite side and of the asymmetrical high enhancement of the malignant area. The multiplanar reconstructions were useful for the estimation of the prostate volume, and allowed better visualization of the periprostatic invasion of the fatty tissue, seminal vesicles, bladder or rectum. MIP and VR (volume rendering) techniques are very useful tools in the discrimination of the abnormalities and in the automatic volume estimation.

**Lymph Node Metastases**

Spiral multislice CT is helpful in looking for metastases to the pelvic lymph nodes. Typically, a dynamic scan with a bolus injection of iodinated contrast medium is used, and nodes 1 cm or larger are considered suspect. Under these conditions, the accuracy of CT
is between 70% and 94%. If the tumor is stage T1 or T2 with a low Gleason score and the serum PSA concentration is <20 ng/mL, the probability of metastases is less than 1%.

Distant Metastases

An almost universal site of CaP spread in advanced disease is the pelvis and lumbar spine. A common rule is to perform a skeletal survey in a patient with a serum PSA concentration >20 ng/mL and in any patient with a stage T3 or T4 of the primary tumor or a tumor with a Gleason score of 8 to 10.

Radionuclide scintigraphy with 99mTc diphosphonate is the method of choice, with whole-body planar imaging as initial exam, but because of the low specificity, SPECT or MRI may be added to characterize lesions. When performing CT, the bone spreading of the tumor is well demonstrated, but a plain film is more accessible, repeatable and cheaper than the other methods and it is useful as a routine exam, the most CaP metastases presenting a bony sclerosing aspect.

The latest approach to local staging is fusion of images from MRI, SPECT, and Computed Tomography (CT) into a three-dimensional image that can be rotated to view the prostate from all angles. However, we think this is an excellent engineering achievement, but too expansive for the most countries and less available than FU, while RTE is spreading and adapted to various types of US devices from different manufacturers. For the bony metastases, we think MRI exam with T1WI and STIR acquisitions could differentiate the fixed, sclerosing old metastases from the new ones (Fig. 32,33,34,35).
**Fig. 0:** NG, 65-year-old: sagittal Doppler US scans in a patient with high PSA level, hard left lobe area on DRE (inferior), but abnormal upper-anterior salient vasculature.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
Fig. 0: NG, 65-year-old: the same case, upper-left peri capsular salient arterial and venous vasculature. Note the prostatic contour, shape and structure without significant abnormalities in these transabdominal Dopper US scans.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
**Fig. 0:** The same case: Sagittal and transversal scans offer automatic determination of the predicted PSA with an elevated value.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
Fig. 0: PO, 73-year-old: large prostate volume due to a benign periurethral hyperplasia, with high predicted PSA, but without salient new vasculature even with a too low gain of color Doppler; the real PSA value was normal, concordant with the Doppler US diagnosis.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
Fig. 0: PG, 69-year-old: the large periurethral benignant hyperplasia is hypoechoic and its estimated automatic volume is useful for the therapeutic approach.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
Fig. 0: NG, 65-year-old: the same case as on Doppler US: T1WI with void-signal vessels on the same location in the left lobe; the puncture-biopsy of the right lobe based on the clinical reason of the DRE was false-negative.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
**Fig. 0:** NG, 65-year-old, the same case: T1WI with void-signal vessels on the same location in the left lobe.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
Fig. 0: NG, 65-year-old, the same case: T2WI with void-signal and more vessels on the same location in the left lobe.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
Fig. 0: NG, 65-year-old, the same case: T2WI with void-signal and more periprostatic vessels on the same location in the left lobe.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
**Fig. 0:** NG, 65-year-old, the same case: STIR with hyposignal on the same location in the left lobe, in an area usually in hypersignal.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
Fig. 0: NG, 65-year-old, the same case: native and post contrast helical multidetector CT presented left side pericapsular prostate accentuated vasculature (a, b, c) and left seminal vesicle hypertrophy (d), similar to the aspect on T1WI (e) and T2WI (f).

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
Fig. 0: MP, 73-Year-old: right iliac sclerosing metastases.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
Fig. 0: Same case: native axial view with incomplete periurethral prostatectomy intended for initial diagnosis of benignant periurethral hyperplasia

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
Fig. 0: The same: native axial CT with a right paravesical lymph-adenopathy and the infiltration of the posterior vesical wall with pseudo-ureterocele on the left side.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
**Fig. 0:** The same case: native acquisition with coronal reconstruction demonstrates the left ureterohydrounephrosis.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
**Fig. 0:** The same case: axial CT demonstrates in the arterial phase the left peri vesical-prostatic enlarged vascular plexus and the prostate enhancement especially in the transitional zone.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
Fig. 0: The same level, in the excretory phase.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
Fig. 0: The same case, arterial phase on the ureteral ostium level, visualizes the right paravesical adenopathy and the enlarged left seminal vesicle enhancement.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
**Fig. 0:** The same level, late excretory phase.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
Fig. 0: The same case, lung metastases.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
Fig. 0: The same case: US of the lungs presenting a normal interstitial aspect (right-side screen) with equidistant horizontal lines parallel to the pleura (the lines "A" Lichtenstein), while the interstitial infiltration (left-side screen) determines the comet-tail artifact with alternative hyper and hypoechoic "tails" perpendicular to the thoracic wall, the lines "B" Lichtenstein, which are pathognomonic.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
Fig. 0: CN, 59-year-old, differential diagnosis: vesical trigone tumor with prostate infiltration and extension towards the left ureteral ostium. Note the salient malignant-type vasculature.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
**Fig. 0:** CN, 59-year-old, differential diagnosis in Doppler US: the same case, illustrating the left juxtavesical enlarged ureter without any fluid motion signal.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
Fig. 0: The same case: left kidney hydronephrosis.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO

Fig. 0: HC, 36-year-old: rectal cancer with a pseudo-kidney shape and prostate infiltration; note the pathological vasculature located mainly into the rectal wall.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
Fig. 0: TI, 73-year-old: huge tumor on Doppler US with uncertain departure organ: apparently, a prostate cancer extensive to the bladder and to the rectum, with an important new vasculature.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
Fig. 0: The same case: the huge volume and the normal PSA level argue for a rectal cancer, proved by the biopsy.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
Fig. 0: MM, 78-year-old: native T1WI with a central mass and anterior periprostatic suspect void-signal vessels.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
Fig. 0: The same case, next slice.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
**Fig. 0:** The same case: the pathological mass presents a rapid enhancement of a paramagnetic contrast agent.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
**Fig. 0:** The same case, next slice: the intense and rapid enhancement is highly suggestive for malignancy.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
**Fig. 0:** MM, 65-year-old: sagittal T1WI visualizes multiple cervical lesions in hyposignal, corresponding to CaP metastases.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
Fig. 0: The same case: same level STIR image presents only C7 salient hypersignal, significant for an active (possible recent) metastase.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
**Fig. 0**: The same case, with similar T1WI lumbar lesions.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
Fig. 0: The same case, STIR acquisition demonstrates at only L2 a bony hypersignal evocating a new lesion in a patient under oncological treatment.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
Conclusion

Although imaging diagnostic methods assist urologists in managing men with suspected or known prostate cancer, much more is needed. Because current methods for determining confined CaP for the individual patient are only "guesstimations" [9], the pathological outcomes for clinically confined CaP have only a 50% probability of being correct.

In Europe, where older patients do not receive treatment for asymptomatic prostate cancer, 85% of them are alive at 5 years, so it is very important to minimize the toxicity of any treatment for PC. As tumor angiogenesis factors potentially play a more important role in the understanding and treatment of prostate cancer [19], imaging flow assessment may become even more important in the diagnosis and the treatment of these patients.

In our experience, the prostate cancer has more vasculature as compared with the non-cancer areas, and that was proved in Doppler US, spiral CT and MRI on the same patient. Even in early stages, when no evident tumor mass was present on the imaging exams, we suspected cancer when the pericapsular vessels were enlarged or presented high flow (Doppler, MRI).

As differential diagnosis, acute prostatitis had more homogeneous increased vasculature and the clinical diagnosis was conclusive, while chronic prostatitis was sometimes similar with the cancer on the clinical exam and native imaging diagnosis but had no vascular changes. Similarly, with acute prostatitis, markedly increased color flow Doppler reflected the severity of inflammatory cellular reaction, but in this case there was usually a diffuse, homogeneous hyper vasculature, as it is seen 24 hours after ejaculation in normal subjects, too [20].

Benign periurethral hyperplasia, known as prostate adenoma, could present sometimes high predicted PSA value on US and eventually high serum PSA level, but the Imaging diagnosis (US, multidetector CT and especially MRI) has good accuracy and we recommend it as the method of first intention, reducing the number of unnecessary biopsies (Fig. 1 on page 64).

Our study has inherent limitations, among them the small number of patients or the technological level of the imaging platforms; however, the utility of the vasculature assessment was demonstrable, even in the cases with DRE/biopsy discordance, or post surgical incomplete lesion removal during the prostatic benignant hyperplasia treatment. It is logically better machines will confirm and improve our results.
MRI had the best sensibility (Fig. 2 on page 64), but we agree Full Prostate Ultrasonography, including Doppler exam in 2D and 3D/4D acquisitions and Sono-Elastography (as a complementary tool) will be soon the best non-invasive, available and low cost imaging method of detection, follow-up and guided target biopsy of the prostate cancer. The limits of the Sono-elastography as wrongly considered an alternative exam were the false-positive findings (275/533 areas; 51.6%) associated with chronic inflammation and atrophy especially at the basal prostate areas [21]. That result the limits of the Sono-Elastography could be eliminated, as in breast US, by the assessment of the local vasculature.
Fig. 0: CC, 78-year-old patient with moderate elevated level of seric PSA: MRI exam in sagittal T2WI (a), T1WI (b), enhanced-T1WI (c) and axial corresponding images (d, e, f) visualizes a benign periurethral hypertrophy, a thin, homogeneous peripheral zone without pathological enhancement and no suspect periprostatic vasculature.

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
Fig. 0: GI, 76-year-old: CaP on the right posterior-lateral peripheral glandular area, unavailable to the DRE: small lesion in hypersignal T2, associated with salient periprostatic vasculature (axial T2-a and T1-b, sagittal T2-c, coronal T2-d, enhanced-T1-e and STIR-f).

© Radiology and Medical Imaging, Prima Medical Imaging Craiova, County Emergency Clinical Hospital of Craiova - Craiova, Dolj/RO
References


Personal Information

Georgescu Aristida-Costinela
Clinical Emergency Hospital Craiova, Romania
Prima Medical Imaging Center Craiova, Romania

aristida_georgescu@yahoo.com