Prostate Cancer – Meeting Clinical Needs by Advanced MRI at Diagnosis and on Follow-Up

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Introduction

Carcinoma of the prostate is the commonest form of human carcinoma, found at autopsy in 30% of men at the age of 50 and in over 80% of men in their 90s. Worldwide, more than 650,000 men are diagnosed with the disease each year accounting for a 10th of all new male cancers. In Europe, the lifetime risk of being diagnosed with prostate cancer is approximately 1 in 13. In 2006, an estimated 234,460 American men were newly diagnosed with prostate cancer, and over 30,000 died of the disease. There is a close association between recent increases in the incidence of prostate cancer and the use of transurethral resection of the prostate (TURP) for treating obstructive lower urinary tract symptoms due to presumed benign prostatic hyperplasia (BPH) and more recently with serum prostatic serum antigen (PSA) testing. Whether there is a real increase in incidence or not, the number of cases of prostate cancer will rise further as the population at risk (older men) grows with lengthening of life expectancy. With the increased use of PSA testing, it has been noted that there has been a gradual downward stage migration (increased incidence of early disease) with the discovery of carcinomas that are possibly not life threatening. Prostate carcinoma thus represents a significant challenge for men's health. This fact has been recently recognized by the US Congress with the recent introduc-

tion of the Prostate Research Imaging and Men's Education (PRIME) act. This act, the first to directly support imaging technologies and in vivo diagnostics for the detection, diagnosis and treatment of prostate cancer, seeks to authorise an investment of USD 600 million over five years to combat this deadly disease with related educational efforts to raise public awareness. There are considerable limitations in current diagnostic and therapy pathways for prostate cancer patients. Only moderate tumor and nodal staging accuracies of imaging tests has resulted in the patchy adoption of MRI into routine patient management particularly at new diagnosis. The fact that prostate cancer is often multicentric and poorly depicted by non-invasive tests has resulted in whole organ rather than specific tumor-directed therapy. With downward stage migration, it is increasingly unclear whether it is necessary to actively treat all diagnosed cases. There is debate on what constitutes clinically important disease encapsulated by the disparity between the approximate 30–40% prevalence of histological prostate cancer in men older than 50 years of age and the 8% of cancers that become clinically significant or the 3% lifetime risk for death from this disease. Since therapies are not without their sometimes devastating complications, there is increasing patient pressure for more minimally invasive and more effective thera-

peutic approaches. In this context it is clear that focal ablations (so-called "male lumpectomy") will play increasingly important management roles (examples include photodynamic therapy (PDT), cryotherapy, high-intensity focused ultrasound (HIFU) and high-dose rate brachytherapy). The usage and future success of these treatments will depend on the identification of clinically significant focal disease (the dominant intra-prostatic lesion (DIL) also called index lesion and the absence of extra prostatic disease (see box for additional clarification of these terms). Additionally, new therapeutic approaches include prophylactic nodal radiotherapy with the intensity modulation (IMRT) require the accurate mapping of the location of pelvic lymph nodes for the eradication of metastases. In the future, patient therapy will be more personalized taking into consideration not only the extent of local disease but also assessments of biological aggressiveness as well as patient and physician preferences. It is in these contexts that this paper describes the current and future roles of MRI in prostate cancer patient management. The approach is from the perspective of the patient pathway describing clinical and research requirements at each stage and the authors' opinions on the roles of morphological and functional imaging in order to overcome current bottlenecks in prostate cancer management. The opinions expressed

Terminology

Localised prostate cancer can be stratified into risk groups using combinations of clinical findings, histopathology using the Gleason grading system and presenting serum prostate specific antigen level (PSA). General risk categories for prostate cancer are given in table 1. Many readers will be unfamiliar with some of the terminology pertaining to prostate cancer management. These concepts are used in different ways by clinicians and pathologists and the authors' current understanding of these terms is as follows:

Dominant intraprostatic lesion (DIL) also called Index lesion: This is a vague term used in the radiotherapy/surgical literature referring to the major focus of disease in terms of tumor volume, the goal being to focally ablate these regions as part of whole prostate gland therapy.

Clinically insignificant disease: Small-volume prostate cancers (usually 0.5 ml or less) without elements of Gleason grade pattern 4 or 5. By definition these tumors are non-palpable and confined to the prostate gland. However, since many prostate cancer deaths occur more than 10 years after the initial diagnosis, the biological behavior of small-volume prostate cancers may become important in patients with relatively long post-diagnosis life expectancies.

Clinically significant disease in non-palpable (T1c) prostate cancer: These tumors are often risk stratified by well-established prognostic factors (Gleason score [GS], pretreatment serum PSA level, and percent positive biopsy findings [%+Bx]) because these factors predict biological aggressiveness.

High risk: GS = 8-10 or PSA level > 20 ng/mL; or GS = 7 or PSA level > 10–20 ng/mL and > 50%+Bx – these patients have a historical four-year PSA control of 10% to 30% after definitive therapy.

Intermediate risk: GS = 7, PSA level > 10–20 ng/mL, and 34%–50%+Bx. These patients have a historical four-year PSA control of 50% to 60% after definitive therapy.

Significant disease can also be based on age and GS. Antiticipated prostate cancer mortality greater than 30% to 50% also includes patients with GS = 7 and age 70 years, and GS = 6 and age 65 years.

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represent the views of the authors based on literature reviews and personal experiences. Recommendations given are partly dependent on our subjective assessments of ease of imaging acquisition, analysis and interpretations.

Roles and current limitations of MRI in clinical practice

From the outset it should be recognised that MRI for newly diagnosed cancer patients is not universally accepted nor used. However, the majority of urological surgeons and radiotherapists agree that the following patients should have MRI at first diagnosis:

1. Symptomatic patients: MRI has an important contributing role in determining tumor extent, detecting complications and planning treatment.
2. Patients at higher risk of local / metastatic spread: a current consensus definition of risk groups for prostate cancer patients is given in table 1.
3. Potential surgical candidates where Partin tables suggest the risk of extraprostatic disease (level of risk is debated but probably > 30% – depending on radiological expertise).
4. Patients with palpable apical tumors. Patients with advanced or metastatic disease need not always undergo detailed local staging with MRI.

It is to be noted that clinical requirements change at various points of the prostate cancer patient's journey and questions for MRI to address are correspondingly altered (Table 2). So for example when MRI is used for newly diagnosed patients, the objectives for its usage are:

1. To delineate the intra- and extra-prostatic extent of the local disease. Here, the key first distinction is organ confinement versus extra-prostatic disease.
2. Prostatic cancer is often multifocal, and the detection of the dominant prostatic cancer nodule or index lesion is becoming important for therapy planning (for definition see box).
3. To detect the presence of cancer at the prostatic apex; this is an important consideration for patients being considered for surgical therapy.
4. To detect the presence and location (intra- versus extra-pelvic) of metastatic nodal involvement.
5. To detect the presence of bone metastases.
6. To detect the presence of complications of urinary tract obstruction.

Years of experience shows that morphological (T2-weighted) MRI has many limitations for the evaluation of the prostate gland. We have come to recognize that tumor volume and distribution is often underestimated because not all tumors are visible and small tumors are not consistently shown. Confounding effects occur because there are other causes of low signal intensity in the peripheral gland

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Table 1: UK National Comprehensive Cancer Network (NCCN) definitions of risk for prostate cancer (2005)

Low Risk	T1-T2a and Gleason Score 2–6 and PSA < 10 ng/ml
Intermediate Risk[1]	T2b-T2b or Gleason Score 7 or PSA 10–20 ng/ml
High Risk[1]	T3a or Gleason Score 8–10 or PSA > 20 ng/ml

[1] Patients with multiple adverse factors may be shifted into the next higher group. Note: T3a/b and T4 disease is not organ confined.

Table 2: The prostate cancer patient journey and contribution of MRI in patient care

Clinical Journey begins here	Suspect cancer	Stage known cancer	Initial observation (deferred therapy)	Curative intent			Palliative	Monitoring effectiveness of therapy	Surveillance of treated disease	Suspect relapse	Treatment of relapsed disease	
				Surgery	Ablative therapies (HIFU, PDT, cryotherapy brachytherapy)	External beam radiotherapy to prostate ± pelvic nodes					Local salvage	Palliative
Clinical scenario	Raised PSA with negative biopsy TRUS and or biopsies	Cancer diagnosed and confirmed by biopsy	Small volume Low aggressiveness	Organ confinement No tumour at prostatic apex No metastases	Organ confinement No metastases	Usually includes neo-adjuvant hormones	Usually hormonal therapy ± RT	Usually after focal therapies	Rare to use imaging in this role (Serum PSA surveillance)	Significant rise in serum PSA	Disease is localised and salvage is possible	Disease is not localised and salvage is impossible
Clinical (C) or Research (R) requirements	Define tumour location and size for targeted biopsy (C)	TNM stage (C) Define dominant lesion (C) Define lesion aggressiveness (C/R) Therapy planning (C)	Confirm organ confinement (C) Document size (C) Depict lesion aggressiveness (C/R)	Detect adverse features (C) Target pelvic nodal dissection (C)	Define dominant lesion location and size (C/R)	Confirm confinement to pelvis (C) Nodal mapping (C/R)	Define extent of nodal & distant metastases (C) Requirements for local palliation (C)	Treatment verification (R) Define volume and extent of residual disease (R)	Detect active disease in absence of significant PSA rise (R)	Identify site and volume of recurrence (C)	Define extent of local disease and absence of metastases (C)	Define extent of of relapsed disease and complications (C) Requirements for local metastases (C)
Contribution made by MRI[1]												
Morphology	+++	+++	+++	+++	+++	+++	++	+++	++	+++	+++	+++
Additional MRI biopsy	+	0	+	0	0	0	0	+	+	++	++	0
Lymphography	0	++	+++	+++	+++	+++	+	0	0	++	++	0
MRSI	+++	+	++	++	+	+	+	0	+++	++	+	0
DW-MRI	+++	++	+++	++	++	++	+	+	++	+++	++	0
Data fusion	++	++	+	++	++	++	0	0	+	+	++	0
DCE-MRI	+++	+	+++	++	+	+	0	+++	+++	+++	+++	0
BOLD-MRI	0	+	0	0	+	+	+	+	0	+	0	0

[1] These authors' opinions are based on literature reviews, personal experiences and recommendations are partly dependent on subjective assessments of ease of imaging data acquisition, analysis and interpretations. *The imaging recommendations are for the purpose of planning therapy.
 0 = No requirement; + = possible requirement; ++ = probably indicated; +++ = definite indication

(scars, prostatitis, haemorrhage and therapy effects) and central gland tumors can be particularly difficult to see in the presence of benign prostate hyperplasia (BPH). Conventionally it was thought that these were unimportant limitations as key therapeutic decisions were based on tumor extent (simply organ confinement or not) but we know that MRI also has a restricted ability to distinguish organ confined disease from early T3 disease resulting in great staging variability from center to center. Furthermore the clinical situation has changed because it is now increasingly important to depict the index lesion/DIL for the application of minimally invasive treatments which may (or may not) be used in combination with conventional approaches. As we move into the arena of personalised patient-oriented therapy, imaging assessments will need to become more comprehensive and accurate, depicting not only the extent of local disease but also assessing biological aggressiveness (by depicting tumor grade other biological important features such as the presence and extent of tumor hypoxia, increased vascularisation and proliferation rate). Beyond local tumor assessments, our current ability to accurately depict nodal metastatic disease is also limited by the use of morphological criteria based mainly on size evaluations. There is a high incidence of reactive pelvic lymph node enlargement and it is well described that adenocarcinoma prostate metastases are of small volume (microscopic) and therefore may be found in normal sized lymph nodes. There is a high incidence of nodal spread to surgically

* Works in progress (WIP). The information about this product is preliminary. The product is under development and not commercially available in the U.S., and its future availability cannot be ensured.

non-sampled sites at pelvic lymph node dissection (PLND). Therefore future assessments of prostate cancer patients will also include more accurate depiction of the presence and extent of nodal metastatic disease.

Overcoming limitations with advanced MRI techniques

Over recent years tremendous experience has been gained in functional MRI techniques and it is becoming increasingly clear that they may be able to address some of the bottlenecks in prostate cancer patient management. New techniques which include dynamic contrast enhanced MRI (DCE-MRI), diffusion-weighted MR imaging (DW-MRI), proton MR spectroscopic imaging (MRSI) and blood oxygen level dependent MR imaging (BOLD-MRI) are making the transition from academic investigation to routine clinical usage. The progress made by each technique in the transition to clinical practice varies, but important lessons on their potential uses and limitations are known. With the advent of faster sequences performed on high-performance, high field strength MRI scanners it is possible to combine morphological and multiple functional prostatic imaging into a more comprehensive evaluation with only a small additional time penalty. Since the limitations of each technique are often non-overlapping it is recommended that multiple functional imaging techniques are used for making diagnoses and therapeutic decisions at various stages of the clinical cancer journey as recommended in tables 2 and 3. The biological basis of observations on these techniques is discussed briefly with appropriate references for interested readers. Examples of multifunctional imaging use in clinically suspected cancer at diagnosis and after definitive treatment are shown in the figures. **Dynamic contrast enhanced MRI** (DCE-MRI) using small molecular weight gadolinium chelates enables non-invasive imaging characterization of prostatic vascularity. Established clinical roles in pros-

tate gland include lesion detection and localization, for tumor staging and for the detection of suspected tumour recurrence [1]. **Diffusion-weighted MRI** (DW-MRI) is a technique that displays information about the extent and direction of random water motion in tissues. DW-MRI provides information on extracellular space tortuosity, tissue cellularity and the integrity of cellular membranes. Clinical data indicates a number of potential roles in prostate cancer including lesion localisation and characterisation and determination of the lesion aggressiveness [2]. Diffusion MRI images should always be interpreted by integration of morphology, high b-value (> 750 sec/mm^2) signal appearances and on ADC maps. This is because the calculated ADC values are dependent on the range of b-values used with additional errors arising from noise in very high b-value images. **MR spectroscopic imaging** (MRSI) of the prostate depicts the altered metabolism associated with prostate cancer. Normal prostatic glandular tissues shows high citrate levels whereas prostate cancer is characterised by high levels of choline. Studies to date suggest that MRSI might provide information that could be used to increase staging accuracy for less experienced readers and thereby reduce inter-observer variability, improve the non-invasive assessment of tumour location (although a recent American College of Radiology Imaging Network (ACRIN) study was inconclusive) and provides guidance for directing biopsies and focal therapies [3,4]. The primary source of image contrast on **Blood Oxygen Level Dependent** MRI is endogenous, paramagnetic deoxyhaemoglobin which increases the transverse relaxation rate (R2*) of water in blood and surrounding tissues and thus BOLD-MRI is sensitive to pO2 within and in tissues adjacent to perfused vessels. BOLD-MRI does

1 **Rising PSA levels with repeated negative TRUS biopsies.**

This 56-year-old male patient had 3 negative transrectal ultrasound (TRUS) guided biopsies for rising serum PSA levels over 2–3 years. In May 2006 the PSA level was 5.8 and now it had risen to 14.6 ng/ml. A multifunctional study was undertaken. Morphology, DW-MRI, DCE-MRI and MRSI examinations were all obtained within a 1-hour examination time on Siemens 1.5T MAGNETOM Symphony scanner with Tim (Total imaging matrix) capability using surface coils only. Evaluations of data obtained were done on Siemens Leonardo Workstation (MMWP) using Viewing, MRP with fusion, MeanCurve and Spectroscopy Taskcards.

1A **Viewing TaskCard. Top-Left:** T2-weigthed image shows some low signal in the peripheral zone at the base of the prostate gland in the midline. No central gland abnormality is shown.
Top-right: ADC map (calculated from b-value 0t, 50t, 100t, 250t, 500t and 750t images) shows restricted diffusion in the left central gland measuring 1.3 cm (arrow).
Bottom-left: Fusion image (b 1200 trace+T2-weighted) with 50% opacity confirms that the restricted diffusion is co-located in the left central gland indicating high cellularity.
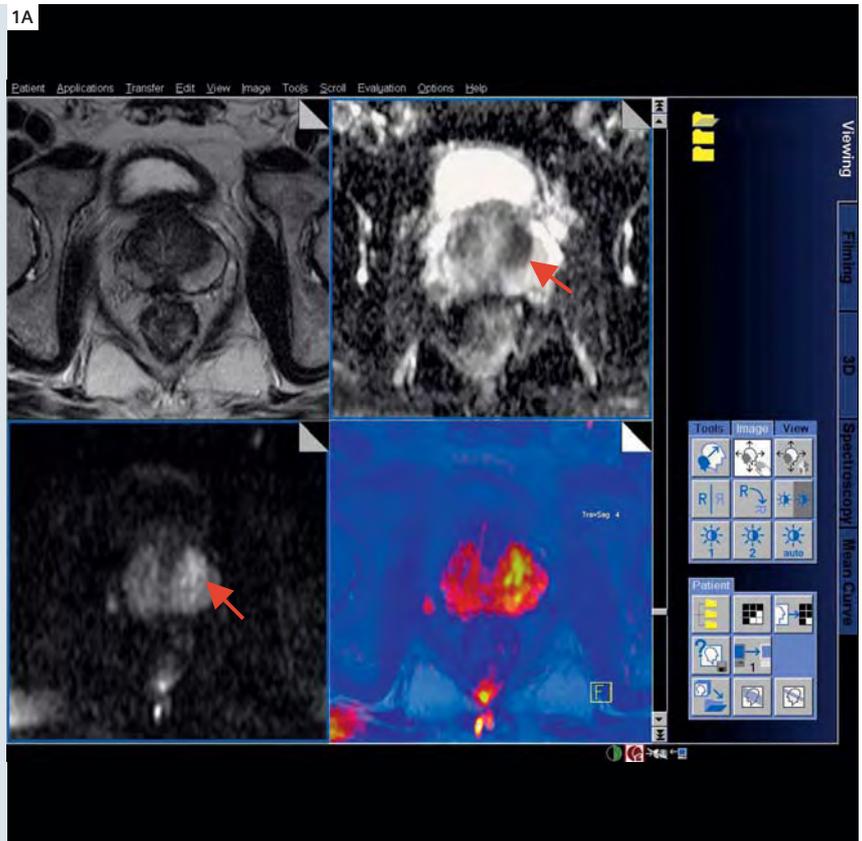
1B **MPR TaskCard.** Anatomical and functional images are co-localised using advanced, non-rigid software algorithms with false colour overlays of high b-value (b1200t) images. The TaskCard shows the prostate in 3 planes and indicates the site of high cellularity which can be used to indicate where to biopsy and can guide focal therapies.
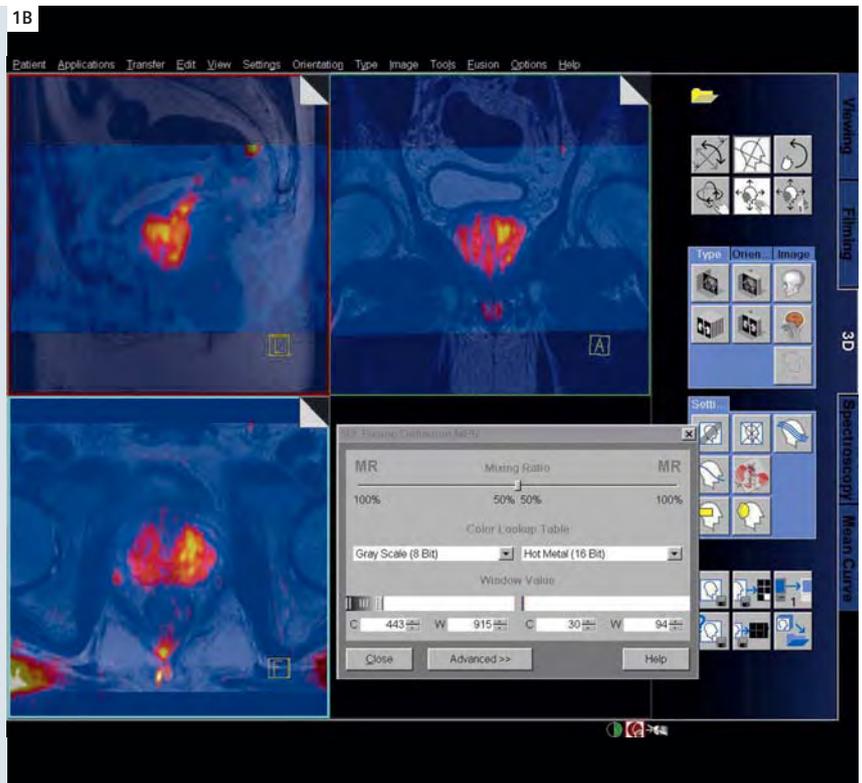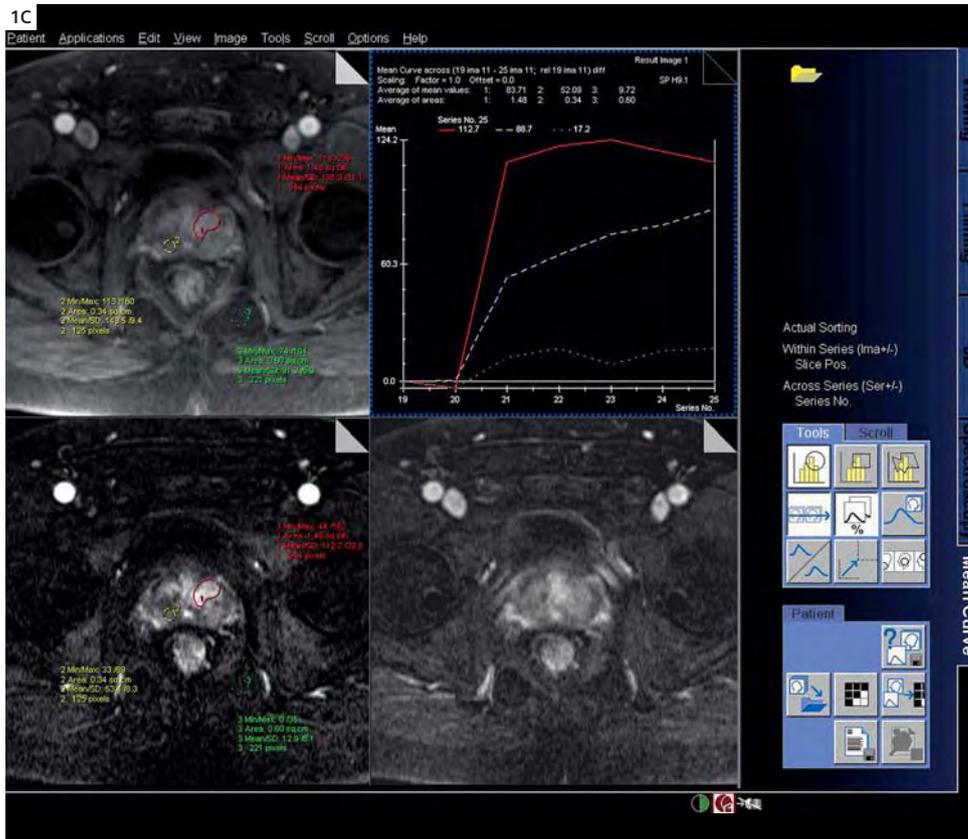
1C The MeanCurve TaskCard can be used to analyze dynamic contrast enhanced images (DCE-MRI). High spatial resolution DCE-MRI data were acquired every 30 seconds (twice before and 5 times post 0.1 mmol/kg Gd-DTPA). **Top-left:** Regions of interest (ROIs) are placed in the region of the restricted diffusion (red ROI), in the right peripheral zone (yellow ROI) and in ischio-rectal fat. **Top-Right:** Graphic depiction of contrast-enhancement with time shows marked early enhancement of the mass in the left central zone with some wash-out (red line). **Bottom-left:** Subtraction image depicts more clearly the enhancing regions and can be used to place ROIs. **Bottom-right:** Late post contrast enhanced T1-weighted image with fat-suppression. The area of high enhancement is difficult to see.
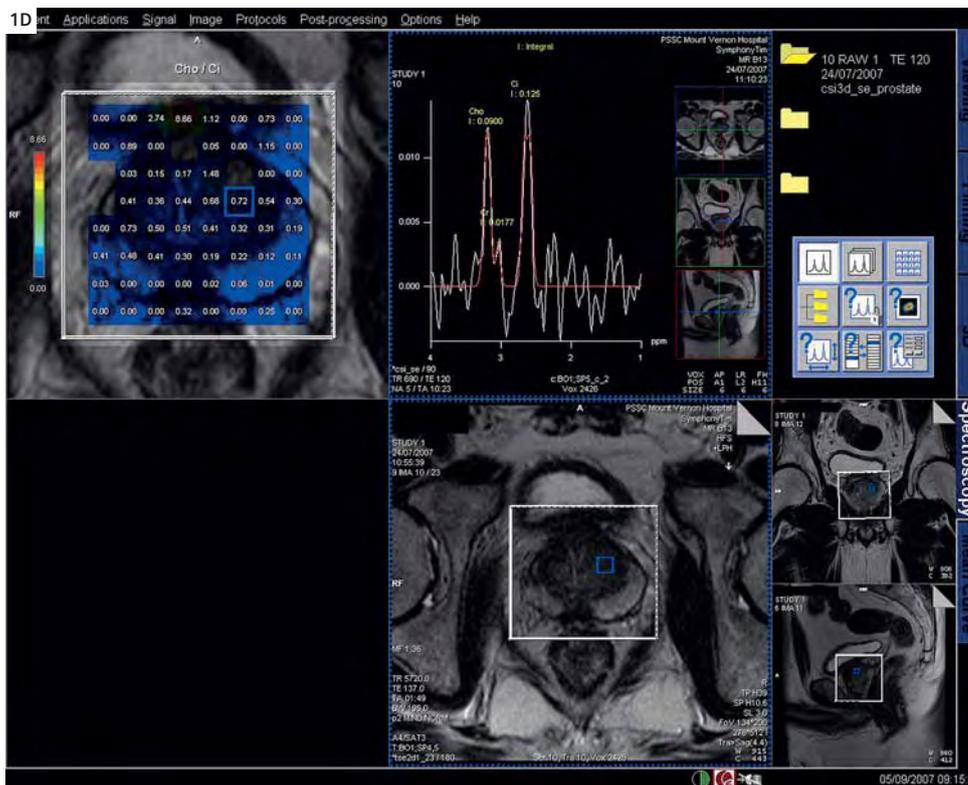
1D Spectroscopy TaskCard. MR spectroscopic imaging (5 x 5 mm voxel) from the left central gland lesion shows abnormal spectrum with high choline and low citrate levels (Choline: citrate ration: 0.72). The information obtained with these tools indicates a highly suspicious lesion suggestive of prostate cancer in the left central gland (mass, high cellularity, high perfusion and abnormal metabolism). This area was specifically targeted for biopsy and a cancer was diagnosed.

*Works in progress (WIP). The information about this product is preliminary. The product is under development and not commercially available in the U.S., and its future availability cannot be ensured.

**2** **Tumor recurrence following radiotherapy**

72-year old male patient with prostate cancer previously treated (4 years prior) with radio-therapy for prostate cancer for T3a/b disease but now with rising serum PSA levels (5.4 ng/ml).

2A **Top-Left:** T2-weighted image showing a 2 cm mass posterior arising from the peripheral gland of the prostate breaching the mesorectal fascia indenting but not invading the rectum.
**Top-Right:** ADC map (from b0-750t images) showing marked restriction of water diffusion in relation to the mass behind the prostate.
Bottom-right: b 1200 trace image shows hyperintensity of the tumor recurrence; note that the treated prostate gland is not hyperintense.
Bottom-left: Fusion image (b1200 trace + T2-weighted) with 50% opacity confirms that the restricted diffusion is co-located in the recurrent tumor.
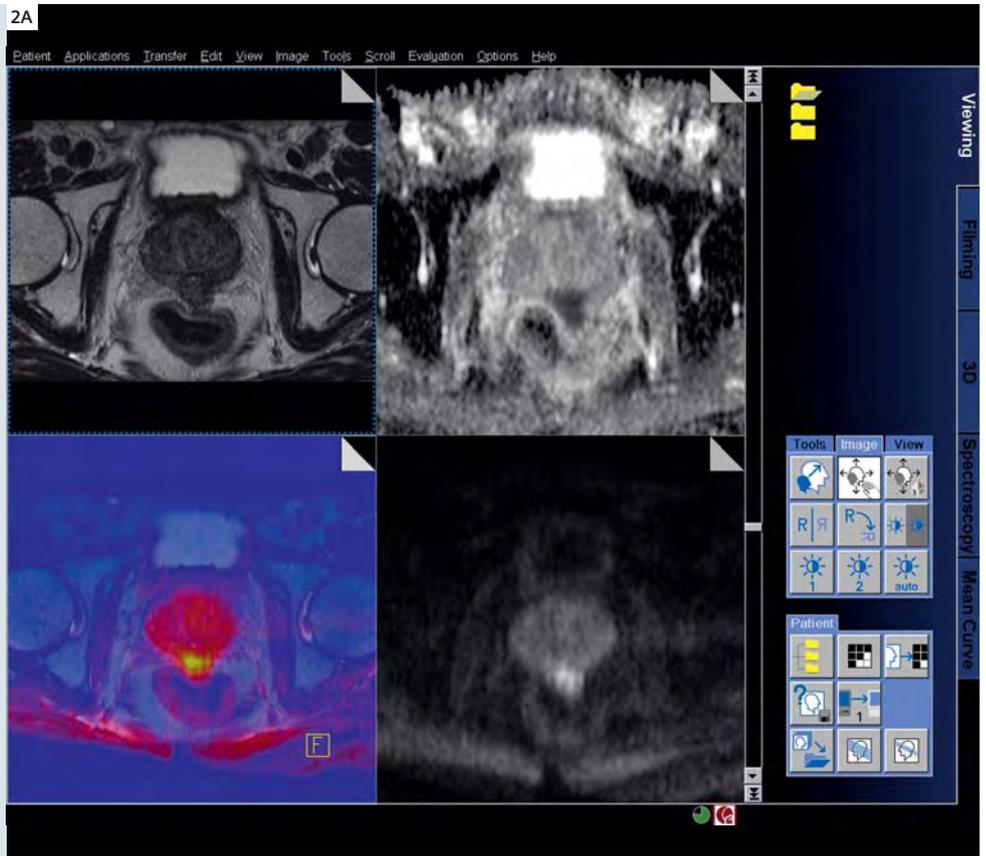
2B Anatomical and functional imaging are co-localised using advanced, non-rigid software algorithms with color overlays of high b-value (b1200t) images in the **MPR TaskCard.** The opacity of the color overlays can be adjusted to optimise data display.
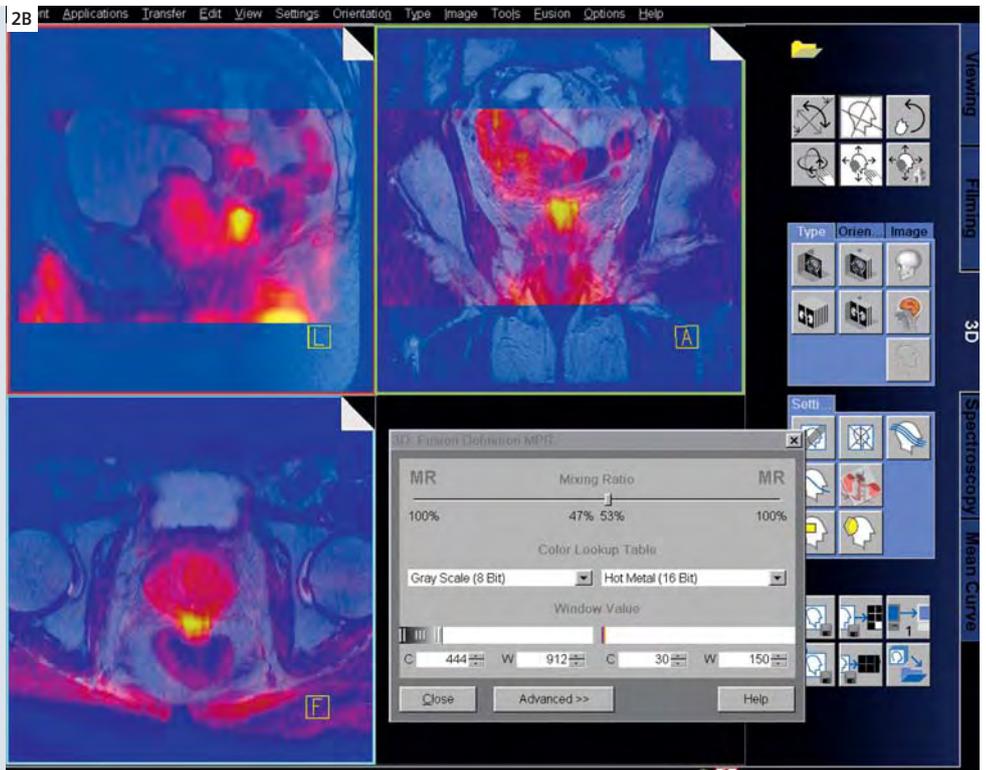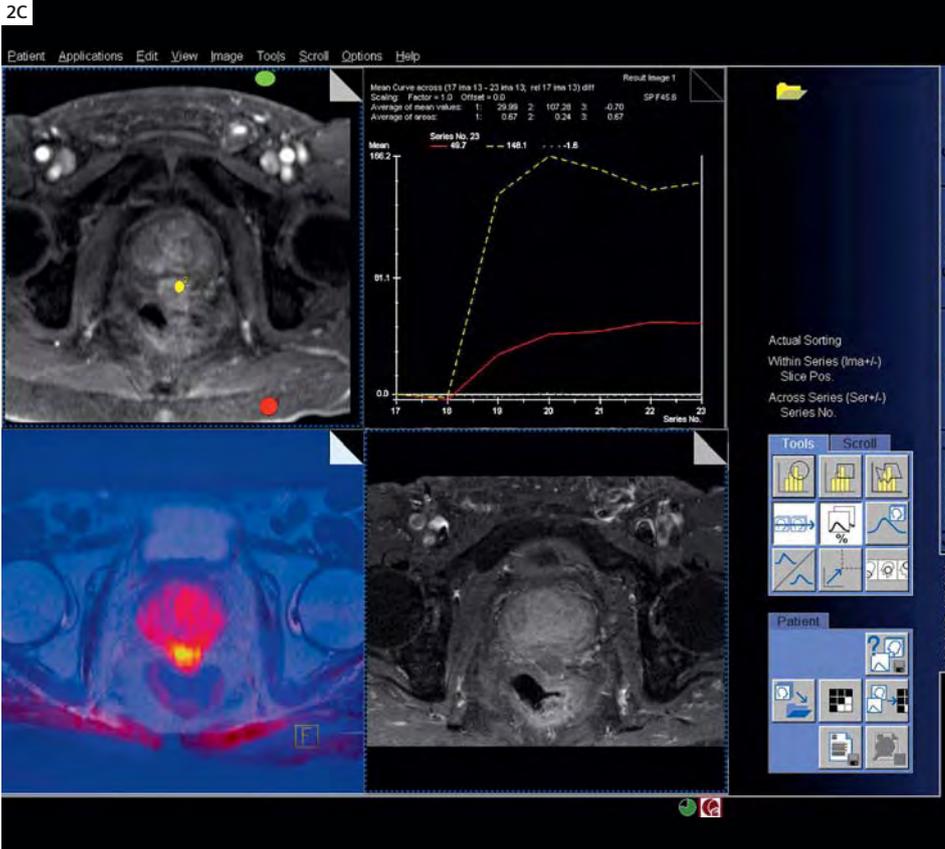
2C This is an example of how the **MeanCurve TaskCard** can be used to analyze dynamic contrast enhanced images (DCE-MRI). High spatial resolution DCE-MRI data were acquired every 30 seconds (twice before and 5 times post 0.1 mmol/kg Gd-DTPA).
Top-left: Regions of interest (ROIs) are placed on the edge of the recurrence (yellow), in fat (red) and in air (green) on the 60 seconds post contrast image.
Top-right: Graphic depiction of contrast-enhancement with time shows marked early enhancement of the tumor recurrence with some wash-out (yellow line).
Bottom-left: Axial fusion image (b 1200 trace + T2-weighted) with 50% opacity.
Bottom-right: Late post contrast enhanced T1-weighted image with fat-suppression. The tumor recurrence is difficult to see.
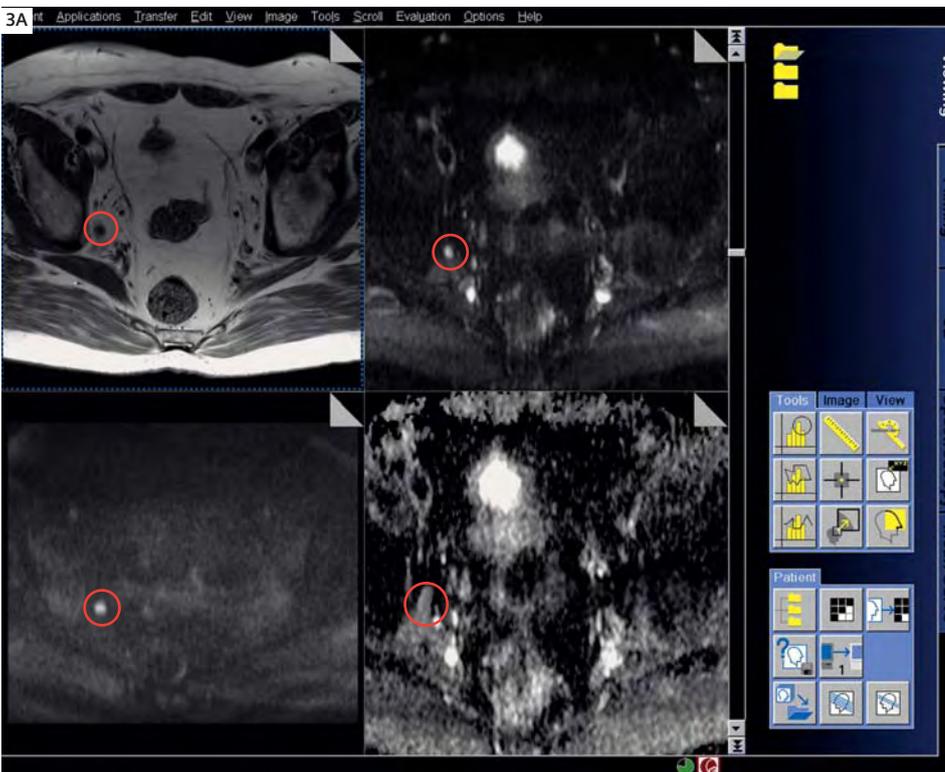
3 **Nodal evaluation with diffusion-weighted MRI**
72-year-old male patient with new diagnosis of prostate cancer. This is the same patient as in figure 5.

3A **Top-left**: There is an equivocally enlarged lymph node (7 mm) in the right internal iliac region (circled).
Top-right: on b0 images, the lymph node is difficult to see because of adjacent hyper-intensity in vascular structures. Note the hyperintense signal in the bladder anteriorly.
Bottom-left: b 1400 trace image shows persistent hyperintensity of the lymph node; all other pelvic structures are no longer hyper-intense.
**Bottom-right:** ADC maps show moderate restriction of water diffusion in the node (1170 x 10^{-5} mm^2/s). Taken together these findings are suggestive of metastatic invasion.

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3B **Top-left** and **bottom-right:**
T2-weighted images confirm the anatomical location of the lymph node in the right internal iliac region.
**Top-right** and **bottom-left:** Fusion images (b 1400 trace + T2-weighted) with 50% and 100% opacities, confirms that the restricted diffusion is co-located in the lymph node.
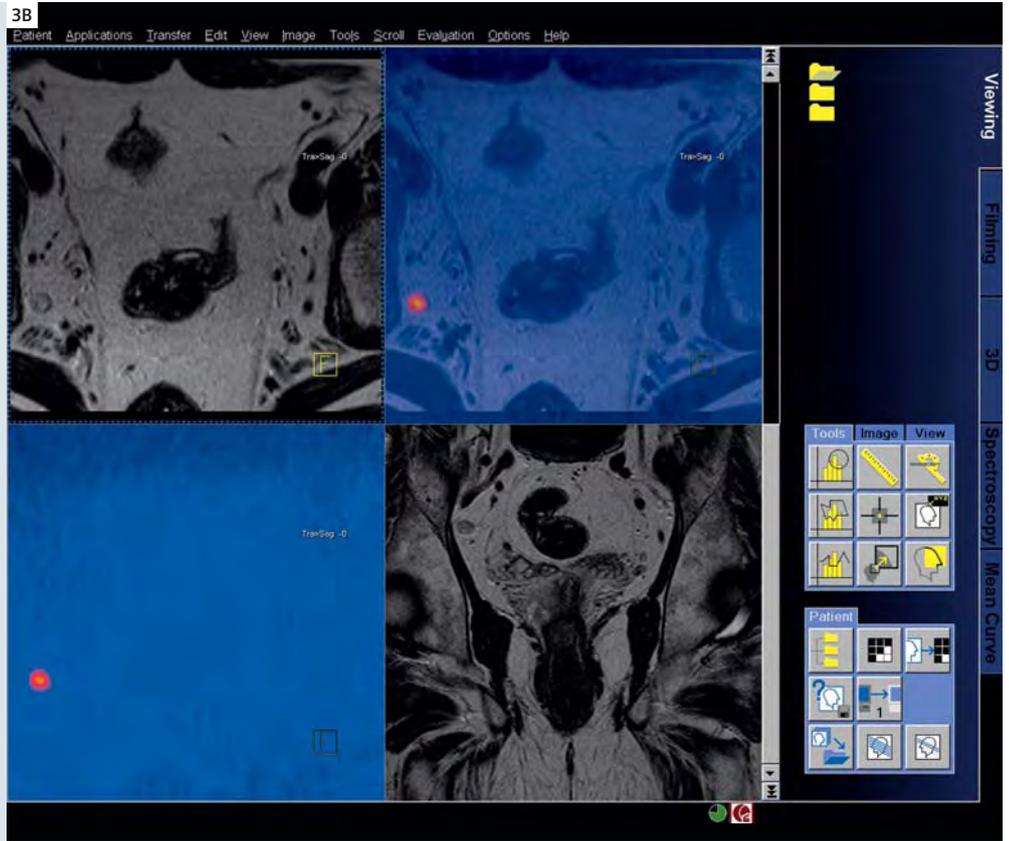

4 **Bone marrow evaluation with diffusion-weighted MRI**
75-year-old male patient with prostate cancer previously treated with radiotherapy for prostate cancer but now with rising PSA levels (2.4 ng/ml). The bone scan was negative and no enlarged lymph nodes were seen. The treated prostate gland had normal appearances post radiotherapy. There are 2 equivocal lesions seen in the bone marrow of the right hemipelvis (straight arrows) with a possible 3rd lesion on the left side shown on the STIR and T1-weighted sequences **(top-left** and **top-right)**.
Bottom-left and **bottom-right:** Fusion images (b 1200 trace + T1-weighted) with 50% and 100% opacities (inverted grey-scale), confirms that the restricted diffusion is co-located in the 2 right sided abnormalities (ADC map not shown). These appearances are highly suggestive of cellular tissues within the bone marrow and therefore of metastases as being the cause of rising PSA levels.
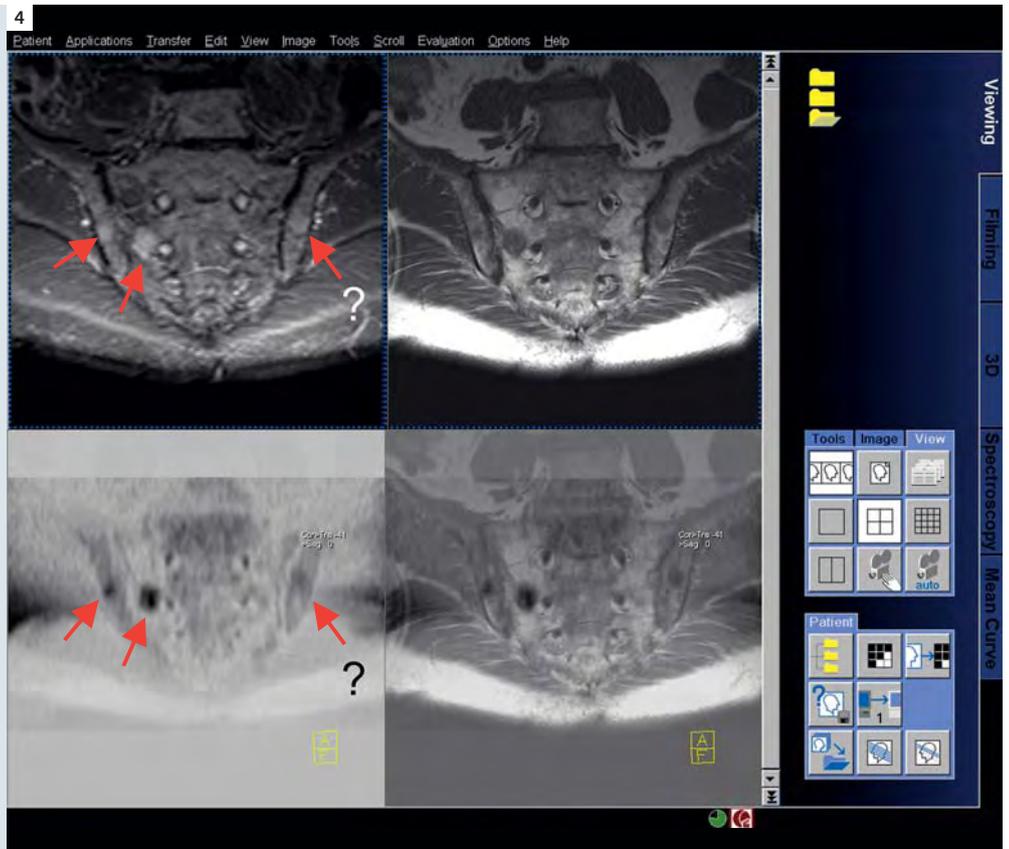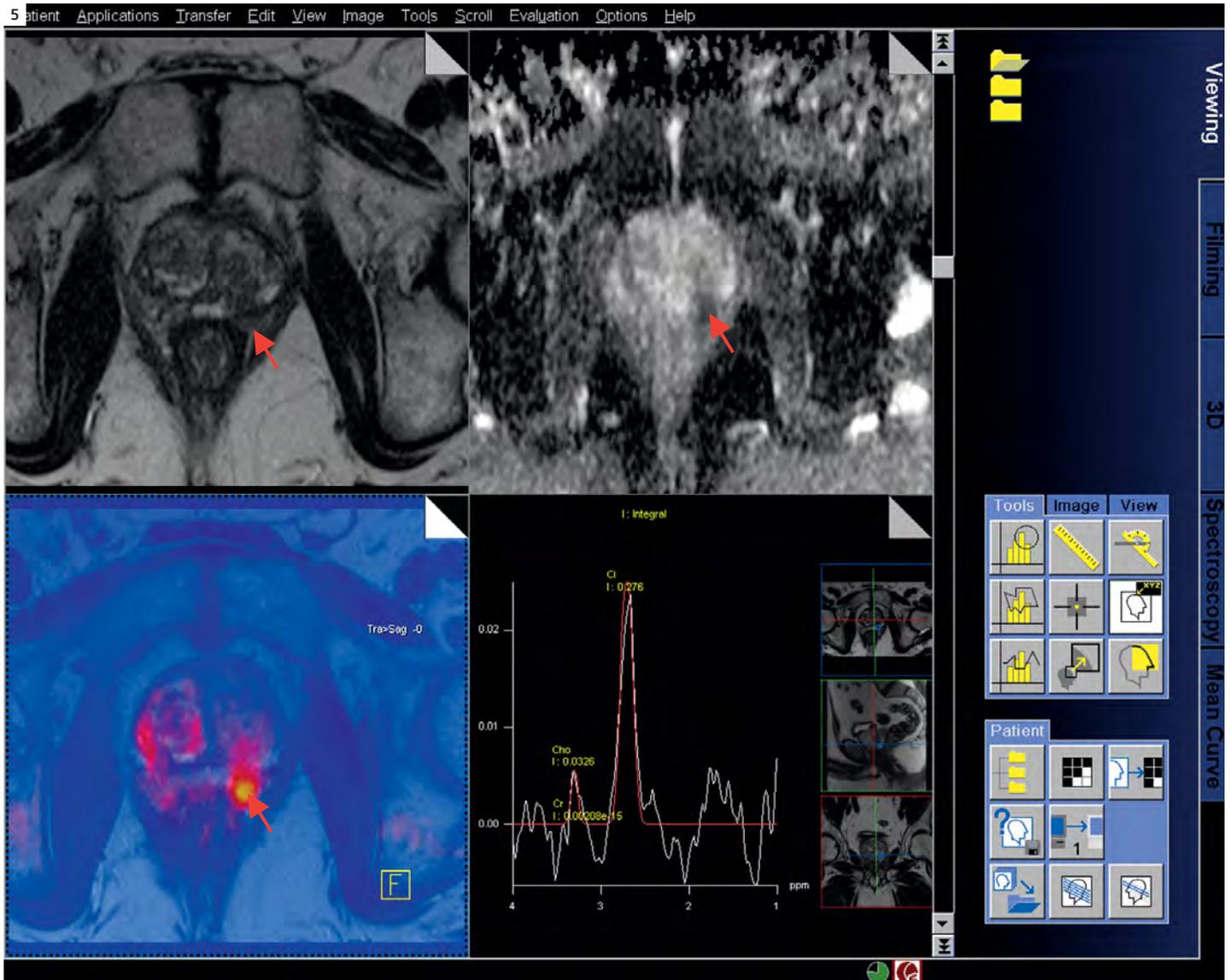
5 **Discordance between DW-MRI and MRSI**
This is the same patient as figure 3. 72-year-old male with new diagnosis of prostate cancer.
Top-left: The T2-weighted image shows moderate volume extra-capsular disease (T3A)
with obliteration of the recto-prostatic angle (arrow).
Top-right: ADC map shows marked restriction of water diffusion in the region of the tumor.
Bottom-left: Fusion image (b 1000 trace + T2-weighted) confirms extraprostatic disease.
Bottom-right: MRSI (5 x 5mm voxel) shows normal spectrum with high citrate and low
choline peaks in tumor.

Table 3: MRI techniques and their usage in prostate cancer patients

Technique (Siemens Tools)	Basis of usage	Indications	Authors' opinions on indication[1]
Morphology (Viewing TaskCard)	Depiction of the tumor extent	At almost every stage of the patient journey (not routinely used for very early stage cancers nor for very advanced disease)	+++
MRI biopsy (None specific)	To obtain histological material targeting a lesion/area Rarely to direct focal treatments to a specified region	Not routinely indicated. Used when cancer is suspected, TRUS biopsies are negative and) MRI depicts suspicious lesion(s)	+
Lymphography with lymph node specific contrast agent (Sinerem/Combidex*) (Lymph Node TaskCard) *Contrast agent not yet approved (Dec 07) but expected soon	To improve the accuracy of nodal staging	Remains to be decided but will include one or more of the following: ■ For newly diagnosed patients who are potentially curable (regardless of therapy modality) taking into account age and volume of disease (including small volume T3 disease) ■ >15% risk for nodal metastases ■ Gleason ≥7 (≥ 4+3) ■ PSA >10 ng/ml regardless of histological grade ■ For nodal mapping prior to IMRT or for targeted, extended PLND ■ PSA relapse – provided local relapse is excluded and bone scan is negative **and** in whom salvage pelvic radiotherapy therapy is being considered	+++
Proton MRSI (Spectroscopy TaskCard)	For depicting the intraprostatic tumor extent For assessing lesion aggressiveness (complementary information to DW-MRI and DCE-MRI and should be used together where possible)	■ For depicting and confirming the location of the primary prostate cancer ■ PSA relapse when bone scan is negative and in whom salvage therapy is being considered	++ ++
DW-MRI (ADC tool)	For depicting the intraprostatic tumour extent (complementary information to DW-MRI and DCE-MRI and should be used together where possible)	■ For depicting and confirming the location of the primary prostate cancer ■ PSA relapse when bone scan is negative and in whom salvage therapy is being considered	++ +++
DCE-MRI with mean curve analysis (DCE and mean curve TaskCards)	For depicting the intraprostatic tumour extent (complementary information to DW-MRI and DCE-MRI and should be used together where possible)	■ For depicting and confirming the location of the primary prostate cancer ■ For monitoring response to hormonal therapy ■ For the assessment of the effectiveness of focal therapies (eg PDT, HIFU) ■ PSA relapse when bone scan is negative and in whom salvage therapy is being considered	++ + +++ +++
Data fusion (MPR TaskCard with fusion option)	Combining & displaying morphological with functional imaging	To aid in the co-localisation for data presentation purposes and for therapy planning. Very useful when used with proton-MRS and DWI.	+++
BOLD-MRI (No specific task card)	To map prostate cancer hypoxia. Used in combination with techniques that map the location of tumours	Could be used for focal ablative therapies as well as radiotherapy planning for boosting dose delivery to hypoxic regions.	+

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0 = No requirement; + = possible requirement; ++ = probably indicated; +++ = definite indication

not measure pO2 directly and in order to be able to correctly interpret BOLD images it is necessary to know or to determine the distribution of blood volume in tissues. Recent data suggests that BOLD-MRI can be used to generate probability bio-maps of prostate tumor hypoxia and when combined with DW-MRI and DCE-MRI may be used to target hypoxic prostate tumor regions with focal therapies such as high dose rate brachytherapy, cryo-therapy as well as HIFU [5, 6].

MR lymphography using the intrave-nously administered contrast agent Feru-moxatan-10 has emerged as a powerful new tool for the evaluation of nodal in-volvement. Much research attesting to its accuracy for nodal characterisation (in-cluding the detection of micrometastases) has appeared in the literature, although efficacy data relating to changing patient management and altering clinical out-comes remains generally lacking [7, 8]. Approval of this contrast agent in Europe is expected soon. Two basic strategies have been explored for **MRI guided pros-tate gland biopsy:** (1) co-registration of previously acquired diagnostic MR imaging to interventional TRUS or open scanner MR images, and (2) stereotactic needle interventions within conventional diagnostic scanners using careful patient positioning or the aid of simple manipu-lators. Such techniques can be used for needle-based interventions for prostate cancer, including biopsy, brachytherapy, and thermal therapy.

Conclusions

As we move into the early 21st century it is clear that the prostate cancer imaging landscape will change radically. One chal-lenge that radiologists will face is how to communicate complex multifunctional information to clinicians looking after pa-tients. One method is to use **fusion tools** which allows anatomical and functional imaging to be co-localised using advanced, non-rigid software algorithms which can also be extremely useful for the purpose of data presentation, analysis, biopsy and therapy planning (examples are shown in figures). Standardized MRI reporting systems depicting graphically the location of abnormalities with the relative confi-dence of diagnostic radiologists will be needed to accurately convey complex information to clinicians. When using such toolbox multifunctional imaging approaches for prostate cancer it is often found that the results obtained are not always concordant (for example, mor-phology, DW-MRI, DCE-MRI may suggest the presence of tumor and MRSI does not – see figure 5 for an example case). The latter is not really surprising as these techniques are depicting different biolog-ical processes. The relative weighting to be placed on each component of a com-prehensive exanimation in a given clinical situation will require sophisticated bioin-formatics approaches where imaging data will be analysed with co-located immuno-histochemistry, gene expression profiles and other biomarker data. We anticipate that fusion of functional imaging and other biomarker data will yield more ro-bust and more effective tumor signatures. Thus, multi-spectral analysis of imaging data represents the new bioinformatics challenge of the early 21st century in prostate cancer.

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