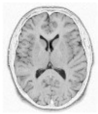


Multi-parametric MRI of the prostate

Belfast Health and Social Care Trust

Northern Ireland Regional Medical Physics Service

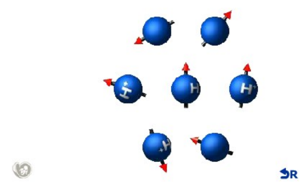
Outline

- Recap of MRI
- T1w, T2w, PD
- Diffusion Weighted Imaging
- Dynamic Contrast Enhanced MRI
- Magnetic Resonance Spectroscopic Imaging
- Putting it all together
- ESUR prostate MRI guidelines 2012
- mpMRI-prostate and Radiotherapy

MRI Recap

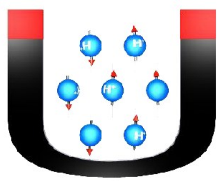
What is MRI?

- In MRI, we are mostly concerned with the hydrogen nucleus, the singly positively charged proton



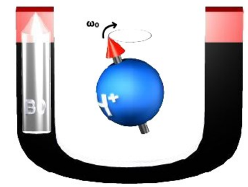
- Other nuclei can be used, but this is mostly in research applications (e.g., ^{3}He, ^{17}O, ^{23}Na, ^{31}P)
- The protons interact with externally applied magnetic fields and radiofrequency pulses

Nuclear Spin in an External Magnetic Field



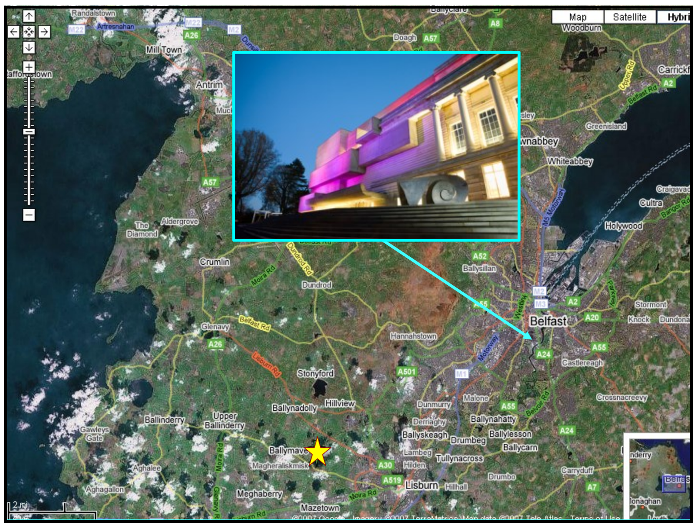
- Within a **large external magnetic field** (called $\mathbf{B_0}$), nuclear spins align with the external field.
- Some of the spins align **with** the field (**parallel**) and some align **against** the field (**anti-parallel**)

Precession Frequency: Larmor Equation

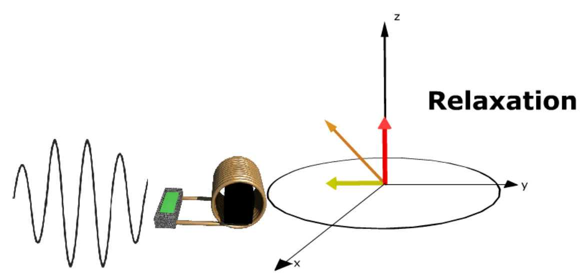


Frequency = 42.6 x magnetic field
(MHz) (T)

Joseph Larmor
Irish physicist
Born in July 1857
in Magheragall, County Antrim
Died 1942
(4 years before the discovery of NMR)



90º RF pulse



T1w and T2w images of the prostate

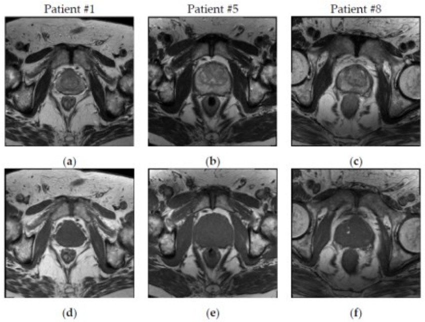


Figure 1. Three instances of input MRI axial slice pairs for the Patients #1, #5 and #8: (**a**–**c**) T2w MR images; and (**d**–**f**) corresponding T1w MR images.

Table 1. Acquisition parameters of the MRI prostate dataset.

MRI Sequence	TR (ms)	TE (ms)	Matrix Size (pixels)	Pixel Spacing (mm)	Slice Thickness (mm)	Interslice Spacing (mm)	Slice Number
T1w	515.3	10	256 × 256	0.703	3	4	18
T2w	3035.6	80	288 × 288	0.625	3	4	18

Rundo et al - Automated Prostate Gland Segmentation - Information 8 49 2017

Diffusion Weighted Imaging

Diffusion

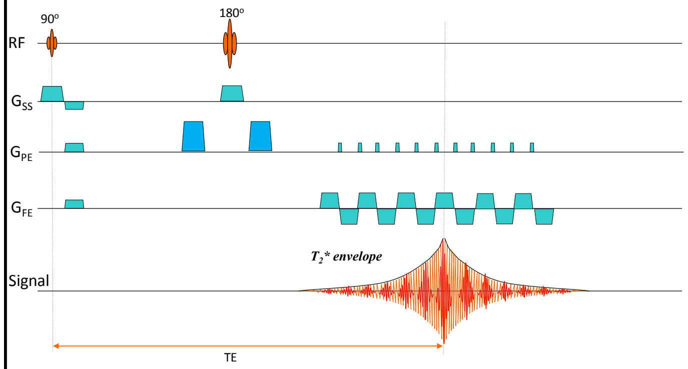
- www.dictionary.com:
    - an intermingling of molecules, ions, etc..., resulting from random thermal agitation, as in the dispersion of a vapour in air
- This random motion sometimes called "Brownian Motion"
- MR signals are sensitive to these random molecular motions
    - **DIFFUSION WEIGHTED IMAGING!**

Diffusion Weighted Imaging

- DWI focuses on the random micro-movements of water molecules inside voxels
- These motions encounter different obstacles in the body (cell membranes, proteins, macromolecules, fibres, ...)
- Obstacles vary according to the tissues and certain pathological modifications (intracellular oedema, abscess, tumours...)
- **Essentially, extracellular water is the main object of exploration in DWI**
- **Diffusion data provides indirect information about the structure surrounding these water molecules**

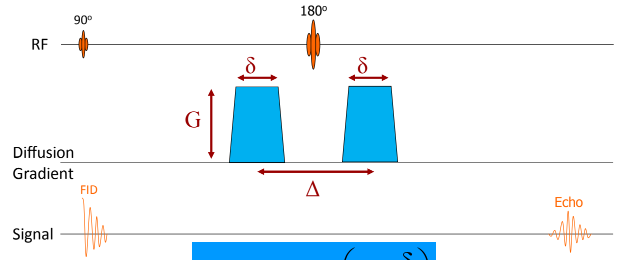
http://www.imaios.com/en/e-Courses/e-MRI/Diffusion-Tensor-Imaging

Diffusion Weighted EPI



Diffusion Weighting

- We can control the amount of diffusion weighting by varying parameters of the gradient pulses



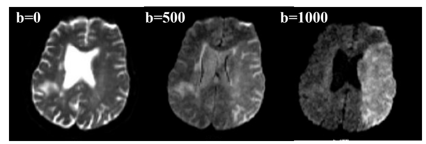
$$b = \gamma^2 G^2 \delta^2 \left(\Delta - \frac{\delta}{3} \right)$$

- The stronger the gradients, the longer they are applied and the more spread out in time, the greater the b-value

Why do these gradients cause diffusion sensitivity?

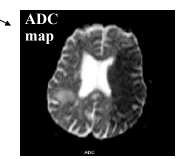
- Remember these gradients have equal and opposite effects!
- If protons are stationary they will experience equal and opposite effects
  - NO NET EFFECT ON SIGNAL
- If the protons have changed location during the time between the two gradient lobes they will experience unequal effects.
- The second gradient lobe cannot undo the effects of the first because the protons have moved
  - DECREASE IN SIGNAL

ADC map



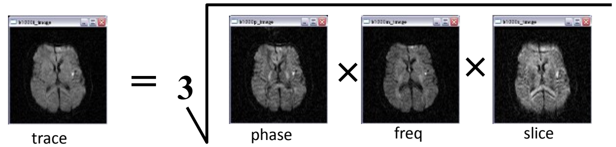
$$S(b) = S(0)\, e^{-bD}$$

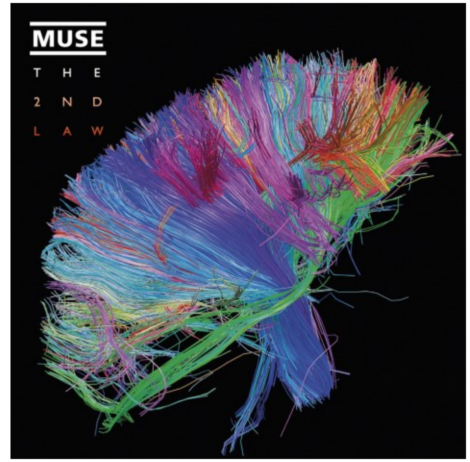
This is done for every pixel



Just a little more complex!

- Diffusion can occur in any direction so we must acquire DW images in at least 3 directions
  - i.e., apply our equal and opposite diffusion gradients in 3 directions
- The geometric mean is taken to yield an "iso-directional" image, sometimes called the trace image.
- Done automatically on scanners
- Can sometimes ask for these directional DW images on the MR operator console





http://en.wikipedia.org/wiki/The_2nd_Law

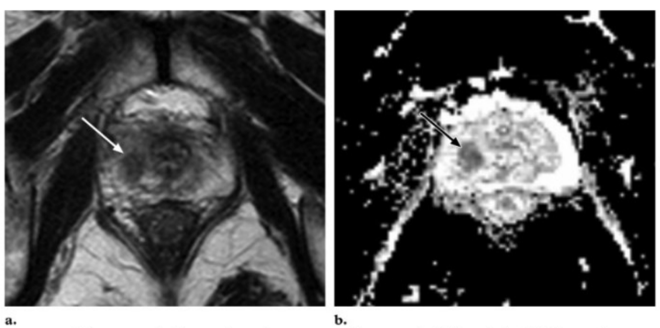


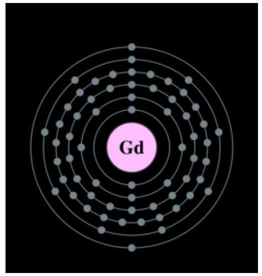
Figure 7. Biopsy-proved adenocarcinoma in a 72-year-old man. **(a)** Axial T2-weighted MR image shows a low-signal-intensity lesion in the right lobe of the prostate (arrow). **(b)** ADC map shows a low ADC value in the lesion (arrow), a finding indicative of decreased diffusion. A targeted biopsy was performed.

Choi et al - Functional Imaging of Prostate Cancer - Radiographics 27 63-77 2007

Dynamic Contrast Enhanced MRI

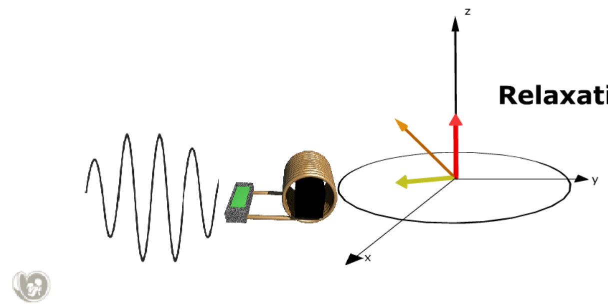
Gadolinium Chelates

- Gadolinium has 7 unpaired electrons
- Strongly paramagnetic
- Toxic in elemental state
- Chelated to a ligand to eliminate/reduce toxicity

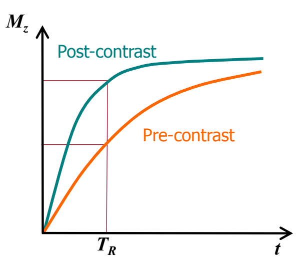


Ground state electron configuration: [Xe].$4f^7.5d^1.6s^2$

90º RF pulse



Contrast Agent shortens T_1



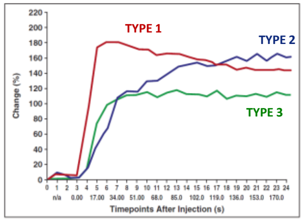
- T_1 relaxation happens more quickly
- M_z recovers faster
- See effect on T_1w images:
  - Shortens T_1, tissue bright

Dynamic Contrast Enhanced MRI - Prostate

- Multiple images taken in time series
- 3D T1w fast spoiled gradient echo
  - High sensitivity to T1 changes
  - Rapid data acquisition (~10s)
  - High SNR
  - Images taken out to 5 minutes
  - Low resolution
- i.v. injection of GBCA
  - Antecubital vein
  - 2-4 ml/s
  - 20 ml saline flush

Why is DCE-MRI data useful?

- Same as other organs, cancer shows earlier and more pronounced enhancement on DCE-MRI
- Aggressive tumours have the ability to initiate an angiogenic “switch” that upregulates molecular pathways leading to tumour angiogenesis
- Number of vessels increase
- Newer vessels have higher permeability (more leaky)
- Analysis of the dynamic enhancement curves
- Malignant lesions show earlier and faster enhancement and earlier contrast agent washout compared healthy prostate tissue



Verma et al - Overview of DCE-MRI in prostate cancer diagnosis and management - AJR 198 1277-88 2012

Prostate DCE-MRI

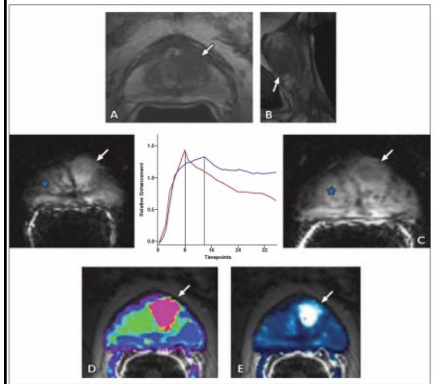


Fig. 3—52-year-old man with prostate cancer of central gland, Gleason score 7 (4 + 3) and prostate-specific antigen level of 19.3 ng/mL who underwent negative transrectal ultrasound prostate biopsy. Endorectal MRI was performed at 3 T for tumor detection. Axial diffusion-weighted image was markedly distorted and nondiagnostic because patient had bilateral hip replacements.

A, Axial T2-weighted image shows ill-defined homogeneous low-signal-intensity mass like region in left central gland (*arrow).*

B, Sagittal T2-weighted image shows homogeneous low-signal-intensity mass far anteriorly in central gland (*arrow).*

C, Early contrast-enhanced T1-weighted gradient-recalled echo image (at peak enhancement) (*right) shows* avid enhancement in left central gland corresponding to T2-weighted abnormality (*arrow). Benign prostate* hypertrophy (BPH) (*asterisk) is seen in right central gland. Kinetic curve (percentage of enhancement over time)* comparison (*center) is made between prostate cancer (red) and BPH (blue). Vertical lines show location of* peak enhancement. BPH shows longer time to peak when compared with prostate cancer. Late enhancement pattern in BPH in this case shows washout, although to lesser degree than in prostate cancer. This example shows that BPH enhancement curves have characteristics that may closely resemble cancerous tissue. Slightly delayed contrast-enhanced T1-weighted gradient-recalled echo image (just past peak enhancement) (*left) shows avid enhancement in entire central gland masking tumor (arrow) (5.8 s/timpoint).*

D and E, Fusion of transverse T2-weighted images with color-encoded maps show utility of color map in identifying tumor. *Ktrans (forward volume transfer constant)* ***(D) and kep (reverse reflux rate constant) (E) maps*** delineate tumor area (*arrow). Pharmacokinetic parameters may be helpful for better differentiation.*

Verma et al - Overview of DCE-MRI in prostate cancer diagnosis and management - AJR 198 1277-88 2012

DWI and DCE-MRI of the prostate

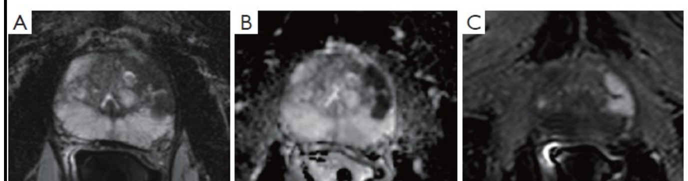
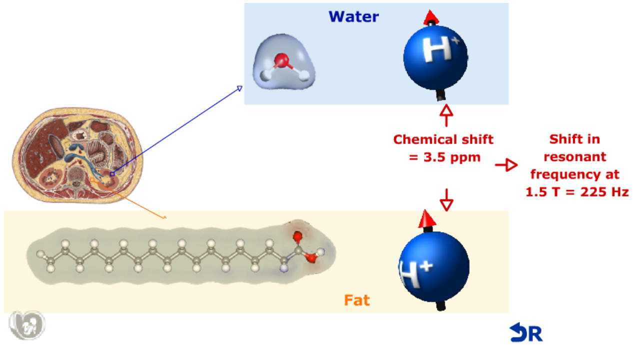


Figure 3 Multiparametric magnetic resonance imaging (mp-MRI) detects significant prostate cancer. This 63-year-old man had a doubling of serum PSA in less than 2 years.
(A) A pseudonodular mass of the anterolateral part of the left mid-peripheral prostate with low signal on T2-weighted imaging (T2WI) is shown;
(B) this mass is associated with low signal on the apparent diffusion coefficient (ADC) map signifying restricted diffusion;
(C) focal asymmetric early enhancement on the arterial phase of the dynamic contrast-enhanced perfusion imaging.
Targeted biopsies of this area revealed high volume Gleason 4+3=7 cancer. PSA, prostate-specific antigen.

Loffroy et al - Current role of mpMRI for prostate cancer - Quant Imag Med Surg 5 754-764 2015

Magnetic Resonance Spectroscopic Imaging

Water and Fat



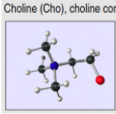
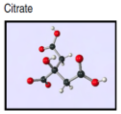
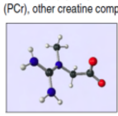
Water / fat protons : different chemical environments slightly different B_0, different resonant frequencies

Chemical Shift

- Chemical shift corresponds to a change in the resonance frequency of the nuclei within the molecules, which is a function of their chemical bonds
- The surrounding electron cloud constitutes an electronic shield that slightly lowers the B_0 field that the nuclei "feel"
- Different electron clouds from different molecules/atoms, hence different metabolites will offer different alterations to the local B_0 field
- Hence, nuclei attached to different molecules will have different Larmor frequencies!

Prostate Metabolites

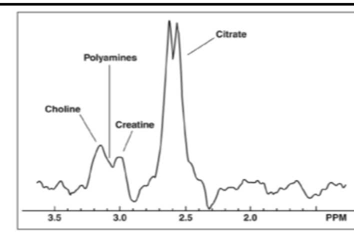
- Carbon - black
- Hydrogen - white
- Oxygen - red
- Nitrogen - blue

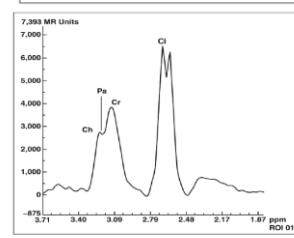
Choline (Cho), choline compounds 	3.24, CH_3, s, -- 3.56, CH_2, t. 7.0 4.07, CH_2, t. 7.0	Choline compounds are present, for example, in the cell membrane and in the synaptic ends of cholinergic neurons. They are part of the lipid metabolism. Increased choline concentrations may mark tumor tissue or multiple sclerosis plaques.
Citrate 	2.60, CH_2, dd, --	Citrate is an important metabolic product of the tricarboxolic acid cycle in the mitochondria of living cells. Intracellular citrate concentrations are low. Citrate can be detected as a secretion product in a normal prostate. A missing citrate signal in prostate tissue might indicate a carcinoma.
Creatine (Cr), phosphocreatine (PCr), other creatine compounds 	3.93, CH_2, s, -- 3.04, CH_3, s, --	When converting the high-energy compound ATP from ADP, PCr is converted to Cr. In brain tissue the signal intensity remains largely constant even in case of pathological changes. However, isolated cases of creatine deficiency may occur in children.

Syngo MR D11, Basic Manual Spectroscopy, Siemens, MR-05002.640.03.02.02

MR Spectra of Prostate

Normal



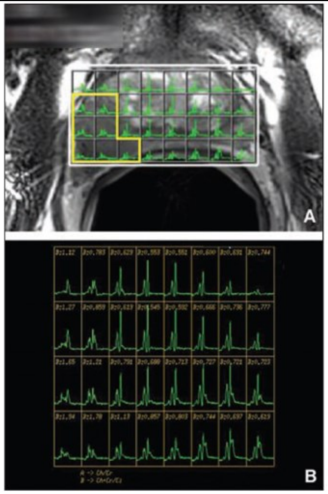


A, 62-year-old man with prostate cancer of Gleason grade 7 (3 + 4).
Ch = choline,
Pa =polyamine,
Cr = creatine,
Ci = citrate.

Verma et al - Prostate MRI and 3D MRS; how we do it - AJR 194 1414-26 2010

MR Spectroscopic Imaging of the Prostate

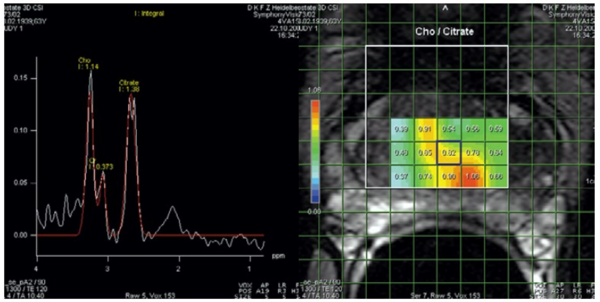
Fig. 12.
62-year-old man with biopsy-proven prostate cancer with prostate-specific antigen level of 6.8 ng/dL and Gleason grade 6 (3 + 3).
A, T2-weighted axial MR image shows 1.7-cm low-signal-intensity mass in right mid gland with prostate capsular bulge.
B, Spectroscopy grid from A shows abnormal ratio of choline and creatine to citrate ratio corresponding to low-signal-intensity mass.



Verma et al - Prostate MRI and 3D MRS; how we do it - AJR 194 1414-26 2010

MR Spectroscopy

CSI: ^{1}H MRS of the prostate



Spectrum of pathological tissue (left) and metabolite image

MR Spectroscopy Quick Guide, Siemens Medical

ESUR prostate MR guidelines 2012

European Society of Urogenital Radiology

Eur Radiol (2012) 22:746–757
DOI 10.1007/s00330-011-2377-y

UROGENITAL

ESUR prostate MR guidelines 2012

Jelle O. Barentsz · Jonathan Richenberg · Richard Clements · Peter Choyke · Sadhna Verma · Geert Villeirs · Olivier Rouviere · Vibeke Logager · Jurgen J. Fütterer

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Abstract The aim was to develop clinical guidelines for multi-parametric MRI of the prostate by a group of prostate MRI experts from the European Society of Urogenital Radiology (ESUR), based on literature evidence and consensus expert opinion. True evidence-based guidelines could not be formulated, but a compromise, reflected by "minimal" and "optimal" requirements has been made. The scope of these ESUR guidelines is to promulgate high quality MRI in acquisition and evaluation with the correct indications for prostate cancer across the whole of Europe and eventually outside Europe. The guidelines for the optimal technique and three protocols for "detection", "staging" and "node and bone" are presented. The use of endorectal coil vs. pelvic phased array coil and 1.5 vs. 3 T is discussed. Clinical indications and a PI-RADS classification for structured reporting are presented.

Key Points

- *This report provides guidelines for magnetic resonance imaging (MRI) in prostate cancer.*
- *Clinical indications, and minimal and optimal imaging acquisition protocols are provided.*
- *A structured reporting system (PI-RADS) is described.*

Keywords Prostate cancer · MRI · Guidelines · Oncology · ESUR

Introduction

In their lifetime, 1 in 6 men will be clinically diagnosed with prostate cancer. This accounts for annually 350,000 cases,

Barentsz et al - ESUR prostate MR guidelines 2012 - Eur Radiol 22 746-757 2012

ESUR prostate MR guidelines 2012

Treatment options: role of MRI

Decisions about imaging patients with newly diagnosed prostate cancer are determined by "intention to treat" (see Table 1).

Low-risk patients Treatment intention is radical surgery, radiotherapy or active surveillance (AS). Mp-MRI can be helpful in managing low risk patients and guide them towards AS, by confirming the absence of significant intra-prostatic disease. Additionally, mp-MRI can be used to help nerve and continence sparing surgery, and to focus radiotherapy.

Barentsz et al - ESUR prostate MR guidelines 2012 - Eur Radiol 22 746-757 2012

Putting it all together

Putting it all together
T2WI, DWI, DCE and MRSI

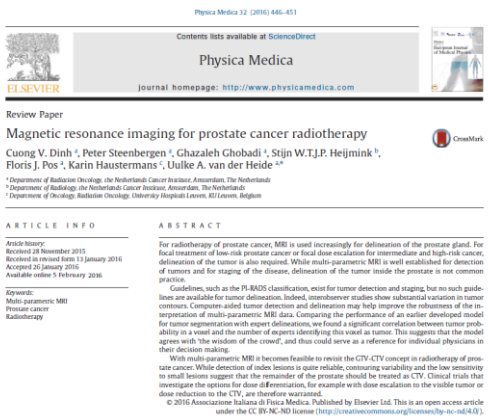
Table 1 Principles and characteristics of T2WI and functional sequences

Sequence	Principle	Finding of prostate cancer	Advantages	Drawbacks
T2WI	Water content of tissue	Low signal intensity	High resolution; sharp demarcation of the prostate capsule	Central or transition zone tumor detection
DWI	Proton diffusion properties	High signal intensity on DWI; low signal intensity on ADC map	Central or transition zone tumor detection; assessment of tumor aggressiveness	Poor resolution and image distortion
DCEI	T1WI with contrast medium	Enhance and wash out rapidly	Local recurrence detection after definite treatment	Long acquisition time
MRSI	Concentration of metabolites	Increased choline plus creatinine/citrate	Assessment of tumor aggressiveness	Needs more expertise; long acquisition time

T2WI, T2-weighted imaging; DWI, diffusion-weighted imaging; ADC, apparent diffusion coefficient; DCEI, dynamic contrast-enhanced imaging; T1WI, T1-weighted imaging; MRSI, magnetic resonance spectroscopy imaging.

Loffroy et al - Current role of mpMRI for prostate cancer - Quant Imag Med Surg 5 754-764 2015

mpMRI-prostate and Radiotherapy



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Review Paper

Magnetic resonance imaging for prostate cancer radiotherapy

Cuong V. Dinh [a], Peter Steenbergen [a], Ghazaleh Ghobadi [a], Stijn W.T.J.P. Heijmink [b], Floris J. Pos [a], Karin Haustermans [c], Uulke A. van der Heide [a,*]

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ABSTRACT

For radiotherapy of prostate cancer, MRI is used increasingly for delineation of the prostate gland. For focal treatment of low-risk prostate cancer or focal dose escalation for intermediate and high-risk cancer, delineation of the tumor is also required. While multi-parametric MRI is well established for detection of tumors and for staging of the disease, delineation of the tumor inside the prostate is not common practice.

Guidelines, such as the PI-RADS classification, exist for tumor detection and staging, but no such guidelines are available for tumor delineation. Indeed, interobserver studies show substantial variation in tumor contours. Computer-aided tumor detection and delineation may help improve the robustness of the interpretation of multi-parametric MRI data. Comparing the performance of an earlier developed model for tumor segmentation with expert delineations, we found a significant correlation between tumor probability in a voxel and the number of experts identifying this voxel as tumor. This suggests that the model agrees with 'the wisdom of the crowd', and thus could serve as a reference for individual physicians in their decision making.

With multi-parametric MRI it becomes feasible to revisit the GTV-CTV concept in radiotherapy of prostate cancer. While detection of index lesions is quite reliable, contouring variability and the low sensitivity to small lesions suggest that the remainder of the prostate should be treated as CTV. Clinical trials that investigate the options for dose differentiation, for example with dose escalation to the visible tumor or dose reduction to the CTV, are therefore warranted.

Dinh et al - MRI for prostate cancer radiotherapy - Physica Medica 32 446-451 2016

Dinh et al.

MRI for prostate cancer radiotherapy

Physica Medica 32 446-451 2016

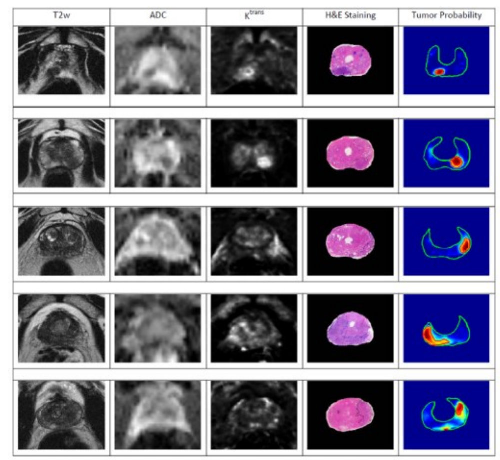


Figure 1. Examples from 5 patients. From left to right: T2w; ADC; K[trans]; H&E staining, tumor probability. The green and red contours in the tumor probability maps represent the peripheral zone region and the estimated tumor area by the model, respectively.

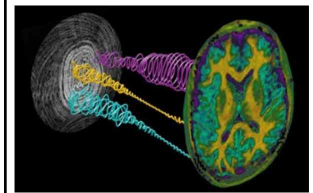
Dinh et al - MRI for prostate cancer radiotherapy - Physica Medica 32 446-451 2016

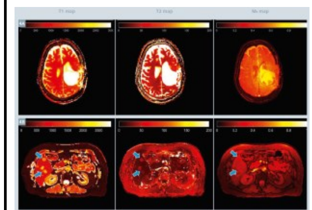
Dinh et al. - MRI for prostate cancer radiotherapy - Physica Medica 32 446-451 2016

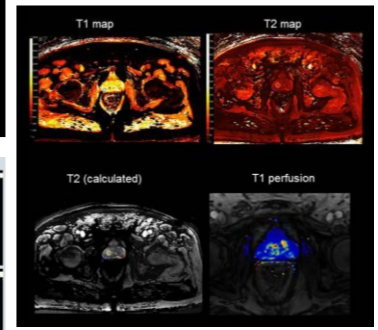
> "With mp-MRI it becomes feasible to revisit the GTV-CTV concept in radiotherapy of prostate cancer. While detection of index lesions is quite reliable, contouring variability and the low sensitivity to small lesions suggest that the remainder of the prostate should be treated as CTV. Clinical trials that investigate the options for dose differentiation, for example, with escalation to the visible tumor or dose reduction to the CTV, are therefore warranted."

Dinh et al - MRI for prostate cancer radiotherapy - Physica Medica 32 446-451 2016

Over the horizon - MR Fingerprinting







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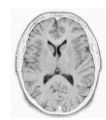

Thanks for your attention

Belfast Health and Social Care Trust

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