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MRI in Diagnosis of Prostate Carcinoma

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Introduction

Carcinoma of Prostrate is a commonly diagnosed tumour in males that represents a broad spectrum of severity, ranging from asymptomatic to highly lethal. The utilisation of prostate-specific antigen (PSA) serum screening has increased the diagnosis of prostate carcinoma. Prostate carcinomas are composed of both indolent and more aggressive carcinomas. The earlier diagnosis of aggressively spreading carcinomas may account for a recent reduction in prostate carcinoma–specific death rates [(1)].

Difficulty with the earlier concept of diagnosis is that elevated PSA values invariably lead to random prostate biopsies, which, in turn, lead to the discovery of incidental, often un symptomatic tumour .Meanwhile, these same random biopsies may miss significant disease. Thus, MRI has a role along with PSA for localisation of biopsy sites and pin pointing those tumours more likely to cause death if left untreated.

In present context, suspicion of prostate adenocarcinoma is primarily based on 3 diagnostic modalities: manual rectal examination by surgeon, Assessment of levels of Prostate specific antigen (PSA) and trans rectal ultrasound (TRUS) . This usually followed by sono -guided biopsies. The latter is recognized by urologists as the first choice in the diagnosis of prostate pathologies. However, all three modern imaging modalities, namely, computer tomography, ultrasonography, and magnetic resonance (MR), have been debated to have limitations in the diagnosing prostate carcinoma [(2)].

Thus, Multi parametric magnetic resonance imaging (mp-MRI) is radiological diagnostic modality of choice in detection of prostate carcinoma. Specifically, multi parametric magnetic resonance imaging (mp-MRI) has been employed in most of contexts. It combines the morphol-ogical assessment of T2-weighted images (T2WI) with diffusion-weighted images (DWI), dynamic contrast-enhanced (DCE) perfusion images and spectroscopic imaging (MRSI) is performed for detection, characterization, and staging for the extent of disease to determine diagnostic or treatment modalities, which can range from guiding to tissue biopsy to prostatectomy [(3)].

T2-weighted MR Imaging

MRI T2 images provides high spatial resolution and defines the anatomical zones and differentiates the peripheral zone from the rest of the zones: central zone,transition zone, ejaculatory ducts, fibromuscular stroma, seminal vesicles andurethra. It also shows the neurovascular bundles. In elderly patients, owing to variable extension of the transition zone due to prostatic enlargement ,signal intensity and size of the prostate transition zone may differ considerably .Benign Prostrate hypertrophy itself is a round, neatly defined, homogeneous area with intermediate signal intensity and a low-signal-intensity rim that encircles the expanded zone of transition .

MRI T1-weighted contrast in the prostate is significantly low. Hence, it is not feasible to appreciate the different anatomic zones on T1-weighted images. In T2-weighted images, prostate carcinoma can show as an area of less signal intensity within the high signal intensity of a normal peripheryzone. The density and the growth pattern of the carcinoma might influence T2-weighted signal intensity. Carcinomas in the peripheral zone, which grow thinly scattered into the surrounding normal tissue, have not shown major difference in quantitative T2 values with normal periphery zone. Whereas, densely growing carcinomas may show lower quantitative T2 values. Low-signal-intensity lesions with a wedge shapes and a diffused extension without mass effect may be reliable signs of tumour being benign . Haemorrhage may be notified on the basis of its high signal intensity on T1-weighted images [(4)].

Limitations exits for T2-weighted imaging has limitations.Focal areas of lower signal intensity in the peripheral zone may not always represent carcinoma. Benign diagnosis like chronic prostatitis, post irradiation or atrophy, scars, hyperplasia, and post biopsy haemorrhage may simulate tumour tissue [(5,6)].

Magnetic resonance spectroscopy imaging

Magnetic resonance spectroscopy imaging permits evaluation of the metabolic activity in the prostate gland through assessing the quantities of different metabolite. In the prostate gland, most commonly found metabolites are choline, creatine, polyamines, citrates. In an otherwise healthy prostate there are lower levels of choline and higher levels of citrates : Opposite is observed in patient with prostate carcinoma.Polyamines may be increased in benign prostatic hyperplasia and reduced in carcinoma. A ratio of choline-plus-creatine to citrate has been widely used to differentiate malignant from benign lesions [(7)].

The role of MRSI in prostate carcinoma detection remains debatable. Previous studies showed no significant difference in specificity and sensitivity for carcinoma detection over standard T2-weighted images. Studies by Testa c et al demonstrated higher sensitivity of MRSI (82 %) when compared with MRI (53 %) but a low specificity [(8)]. Another study by Khaji Y demonstrated a significant improvement in the accuracy of MRSI when combined with standard MRI.MRSI has a similar accuracy in the detection of carcinoma as sextant biopsy, but is more sensitive in the detection of carcinomas of prostate apex, which are frequently missed by biopsy [(9)].

3-Dimensional MRSI has been shown to be helpful in the accurate assessment of carcinoma volume and diagnosis of extracapsular extension by less experienced radiologist. In another study, Westhpalen *et al* reported that MRSI significantly improved the characterization of prostate nodules in the periphery zone [(10)]. In study by Joshep they found it can also predict carcinoma recurrence and response to therapy [(11)].

Magnetic resonance spectroscopy imaging has a potential use as a noninvasive modality to assess prostate carcinoma aggressiveness; choline and creatine to citrate ratio tends to increase with tumour of higher grade, and tumour volume correlates with pathologic Gleason score. The sensitivity of MRSI is approximately 86% for the detection of tumours of Gleason score of seven or

above, but decreases to 45% for a Gleason score of six [12].

MRSI of the prostate is commonly performed with a combination of point-resolved spectroscopy (PRESS) volume localization and 3Dimensional chemical shift imaging. Parameters are chosen to obtain 3Dimensional chemical shift images from as much of the prostate as possible. Though most malignant tumour occur in the posterior aspect of the prostate, a large number of malignant tumours which are missed at ultrasound-guided biopsy occur in the anterior and lateral aspects. Hence , it is important to have adequate spectral coverage of these areas. 3D CSI needs phase encoding in 3 dimensions, traditionally known as frequency, phase, and slice. Acquisition time and coverage of the prostate are the primary considerations in selecting the matrix dimensions. Although it is not absolutely necessary, the most followed approach in selecting the FOV and the spacing parameters is to prescribe isotropic CSI voxels. The in-plane CSI voxel size is defined by the FOV divided by the corresponding direction in the phase coding matrix.

Amith Sukla et al conducted a study to characterize benign and malignant prostate peripheral zone tissue retrospectively by using a commercial magnetic resonance (MR) spectrosc-opic imaging package and incorporating the choline plus creatine–to-citrate ratio and polyamine (PA) information into a statistically based voxel classification procedure. They found statistically based classification rule developed indicated that PAs have an important role in the detection of PZ prostate carcinoma [13].

Dynamic Contrast-enhanced MR Imaging

DCE-MRI has become an significant component of the multiparametric strategy and it is emerging as a useful clinical technique for evaluating the severity, location, and extent of primary and recurrent prostate carcinoma. This technique is different from rest of functional MRI technique as it uses an exogenous contrast agent (low-molecular-weight gadolinium chelate) to assess vascular genesis of tumour.

Prostate carcinoma shows earlier and more pronounced enhancement than surrounding normal prostate tissue on DCE-MRI. This enhancement pattern is may be related to tumour angiogenesis. Aggressive tumours have the ability to initiate an angiogenic code that up regulates molecular pathway, leading to the production and release of various angiogenic factors, like vascular permeability factor or vascular endothelial growth factor. As a consequence, the number of vessels increases and these newly formed tumour vessels have high permeability than the normal vessels due to of weak integrity of the vessel wall .In general, tumour vessels are more permeable than healthy vessels and more heterogeneous in size and more unorganized. Research suggest that the prognosis worsens as the number of abnormal vessels in prostate carcinoma increases [14].

The application of DCE-MRI for prostate carcinoma is based on factual data showing that malignant lesions depicting earlier and faster enhancement and earlier contrast agent washout compared with normal prostate tissues [15]. This requires fast bolus administration of contrast media combined with rapid acquisition methods.

DCE-MRI requires the use of serial 3Dimensional acquisitions before, during, and after a bolus of low-molecular-weight gadolinium contrast media, via the larger vein, using an injection rate of 3 –4 mL/s followed by a 25-mL saline flush. Intra venous injected contrast agents pass from the arteries to the tissue microvasculature and extravagate within seconds to the extravascular extracellular space. Extracellular space is also called the “leakage area.” Contrast agents in vessels and extracellular space reduce local relaxation times, leading to sudden brightening of signal on T1-weighted image sequences. However, the ability to measure vessel leakiness is in part related to blood flow (It is difficult to identify leaking if the flow is very low). This way, the signal measured on DCE-MRI represents perfusion and permeability. A fast injection rate of

the contrast agent captured with fast 3-Dimensional acquisitions ensures that early enhancement within prostate tumours relative to background may be detected. DCE-MRI is sensitive to alterations in vessel permeability, extracellular space, and blood flow [16].

Analysis of DCE-MRI

Qualitative analysis

The qualitative analysis of DCE-MRI and its use for prostate imaging is based on the premise that tumour vessels are leaking and readily enhance after intravenous contrast material is expressed by a faster exchange of blood and contrast media between the capillary and tumour tissue.

Semi quantitative analysis

The semi quantitative approach is also based on the premise of early and intense enhancement and washout as a predictor of malignant tumour.

Quantitative approach

It is based on premise of concentration change of the contrast agent using pharmacokinetical modelling technique.

Jakson et al analysed the ability of DCE-MRI to correctly localise prostate tumour in different ways. Research found that, for one radiologist using a commercial software, DCE-MRI resulted in superior tumour localization compared with T2W scans. They have demonstrated that tumours appear to have different enhancement property to benign peripheral zone and according to ROC analysis, this may results in a diagnostic test which would be considered of fairly discrimina-tory value by conventionally accepted criteria [17].

Sung Y.S et al studied the importance of computer-aided diagnosis for prostate carcinoma detection on dynamic contrast-enhanced MRI (DCE-MRI). Research found accuracy, sensitivity, and specificity of CAD were 84%, 78%, and 78%, respectively, in the entire prostate; 78%, 89%, and 63 %, respectively, in the transitional zone; and 88%, 87%, and 88%, respectively, in the peripheral zone. Values for k(ep), k(el), initial slope, slope , wash-in rate, washout rate, and time to peak showed greater area under the curve values (0.805-0.887) than did the other parameters (0.543-0.664) (p value < 0.01) and were compared with values for CAD. In the entire prostate mass , accuracy was greater for CAD than for all perfusion parameters or T2WI (68 -76%); sensitivity was higher for CAD than for T2WI, initial slope, wash-in rate, slope , and washout rate (39-78%); and specificity was greater for CAD than for T2WI, k(ep), k(el), and time to peak (57-69%) ($p < 0.01$). Reseach concluded CAD can improve the diagnostic performance of DCE-MRI in prostate carcinoma detection, which may vary according to zone anatomy [18].

In a research by Sayed Zidan et al in 2015 , they found sensitivity of DCE-MRI, ADC at 1.2 and ADC at 1.4 in detection of prostatic carcinoma was 99 %, 84.7% and 99% respectively ($P = 0.0001$). The highest validity for carcinoma prostate is DCE-MRI (Kappa = 0.94) followed by ADC at 1.4 (Kappa = 0.87) then ADC at 1.2 (Kappa = 0.78). They concluded that DCE-MRI and DWI have high sensitivity to differentiate carcinomatous from non-carcinomatous prostatic tissue, and the combination techniques may increase the diagnostic accuracy of prostatic carcinoma one alone [19].

DW MRI

DW-MRI has the capacity to represent the water diffusion molecules by the apparent diffusion coefficient, which can directly reflects tissue cellularity. DW-MRI is characterised by a short acquisition time without the administration of contrast medium. Thus, DW-MRI has the potential to become a noninvasive diagnostic method for tumour detection and localisation, tumour aggressiveness, local staging and local recurrence after various therapies. Accordingly, radiologists recognise the principles of DW-MRI, the methods of image acquisition and the pitfalls of image analysis.

In study by Assim Afaaq in 2011, they found that DW-MRI can be easily acquired on a modern

scanner along with a shorter image acquisition time and without explicit need for intra venous contrast mediums. The image contrast is based on the diffusion of water molecule and thus reflects tissue cellularity. There is increasing evidence that DW- MRI improves the sensitivity and specificity of prostate carcinoma detection as well as the identification of tumour aggressiveness. DW-MRI is also showing substantial promise as a response bio-marker for both local and metastatic disease. DW-MRI is proving to be a useful adjunct to conventional T2-weighted MRI sequences. Study concluded eventual role of DW-MRI in combination with other MRI techniques for multiparametric assessment of prostate carcinoma needs to be defined further [(20)].

Ginarini G et al reviewed the literature on potential and limitations of DW MRI in prostrate carcinoma. They concluded, DW-MRI applied in addition to conventional T2 weighted and contrast enhanced magnetic resonance imaging (MRI) improves tumour detection and localisation. In addition, it has shown promise for the assessment of tumour aggressiveness and for treatment monitoring during active surveillance, radiation therapy, and focal therapy. They concluded that W-MRI holds promise to ameliorate the management of patients with kidney, prostate, and bladder carcinoma including pelvic lymph node staging. Present limitations include the lack of standardisation of the technique across multiple centres and the still limited expertise [(21)].

Massom B et al compared T2-weighted MRI alone and T2 combined with diffusion-weighted imaging (DWI) for the localization of prostate carcinoma. Study found that in the peripheral zone, the Az value was significantly higher ($p = 0.003$) for T2 plus DWI ($Az = 0.88$) than for T2 imaging alone ($Az = 0.82$). Performance was poorer in the transition zone for both T2 plus DWI ($Az = 0.76$) and T2 ($Az = 0.78$). For the whole prostate, sensitivity was significantly higher ($p < 0.005$) with T2 plus DWI (83% [120/148]) than with T2 imaging alone (53% [82/149]), with T2 plus DWI showing only a slight loss in specificity compared with T2 imaging alone (83% [204/243] vs 92% [222/244], respectively).They concluded Combined T2 and DWI MRI is preferable than T2 imaging alone in the detection of significant carcinoma (Gleason score ≥ 6 and diameter > 4 mm) within the peripheral zone of the prostate [(22)].

Nuoha Mohahmed et al studied the role of T2WI combined with diffusion WI (DWI) in the evaluation of patients with prostate carcinoma. 38 men were examined and there after T2WI, DWI, ADC map and ADC values were assessed. T2 low SI was detected in the peripheral zone of the prostate of 36 patients, and restricted diffusion in 32 patients. Study concluded that that the addition of the ADC map and DWI to T2WI provide significantly more accurate results for prostate carcinoma detection and staging [(23)].

Standardization of DW-MRI protocol

It is widely argued in literature which could be the best value for prostate carcinoma detection in order to highlight the tumour tissue, reducing the signal from benign prostate tissue, in order to obtain good quality ADC maps for better measurement and visual imaging interpretation without increasing the acquisition time or reduce the signal to-noise ratio.

Kim K et al. and Kou et al. in their research reported a -value of 1000 s/mm^2 showing higher sensitivity of the ADC maps obtained at a -value of 1000 s/mm^2 than those obtained with a -value of 2000 s/mm^2. Regarding the specificity, Kim K et al. stated no significant difference between the two -values (24). Kou et al. demonstrated a higher specificity of the ADC maps obtained with a value of 2000 s/mm^2 when compared with those obtained at a -value of 1000 s/mm^2 [(25,26)].

Kathahera et al and A. B. Rozenkrants et al analysing native DW images, showed that as preferable the use of a -value of 2000 s/ mm^2 compared to a -value of 1000 s/mm^2. Matens et al underlines that native DW images with a -value of 2000 s/mm^2 have higher contrast-to-noise

ratio when compare to a value of 1000 s/mm^2 but less than those with a -value of 1500 s/mm^2 [27,28].

Regarding qualitative analysis of DW images, the use of higher -values is useful for less experienced radiologist; best signal suppression of benign prostate tissue and greater evidence of signal restriction with a higher -value allow an immediate diagnostic evaluation of the images. Images with a value of 1000 s/mm^{2}cannot suppress benign tissue in the PZ and sometimes obscure tumour lesions due to persistent T2-shine-through effects .This context needs to be elucidated as the greater spread of prostate carcinomas needs an increase in MRI examinations for diagnosis, local staging, lesions targeting for biopsy, or focal therapy, so that the analysis of the mp-MRI must be easy in practice, without the need of greater experience [29,30].

As for quantitative evaluation with ADC maps, a higher diagnostic accuracy was obtained with a value of 2000 s/mm^2 when compared to 1000 s/mm^2, though it was not statistically significant. The value of ADC for both benign and pathological tissues when the -value used increases. ADC measurements cannot differentiate low-grade tumours from benign tissue. But that is not a problem because mp-MRI of the prostate aims to detect clinically significant tumours. It is therefore significant to emphasize that our study, in agreement with other studies, shows that ADC value in both PZ and transitional zone (TZ) is lower in intermediate or high grade tumours (Gleason $\geq 3 + 3$) compared to benign tissue [31,32].

How Does Dw MRI helps?

Mechanism by which DWI adds diagnostic accuracy to T2 imaging is not certain. T2 signal loss in the peripheral zone may be related to a number of causes, including carcinoma, inflamm-ation, fibrosis, and haemorrhage. It may that the ADC value is more drastically altered by carcinoma than it is by factors such as haemor-rhage, inflammation, or fibrosis. The cause of lower ADC values in prostate carcinoma may be related to the many tightly packed glandular elements found in carcinomas that locally replace the fluid-containing peripheral zone duct. This could result in a local drop in the ADC values. The different nature of ADC and T2-weighted tissue contrast in the prostate are supported by studies showing no significant correlation between quantitative T2 measurement and ADC values in the prostate. Another reason for the improved performance of DWI might be the quantitation of ADC, which theoretically eliminates the effect of T2 signal variations as well as receiver gain and coil intensity profiles from the image, thereby allowing fixed window levels for assessment. Earlier studies have shown ADC values to be lower in prostate carcinoma, ranging from 1,100 to 1,340 $\times 10^{-6}$ mm^2/s with b values of 300-1,000 mm^2/s compared with normal peripheral zone values of 1,610-1,680 $\times 10^{-6}$ mm^2/s [33,34].

Localisation of prostate carcinoma is important given the emergence of disease-targeted therapies, such as intensity modulated radiation therapy, interstitial brachytherapy, and cryosurgery, as part of care. Knowledge of the tumour location within the prostate can help direct maximal therapy to the largest focus of tumours while minimising damage to the surrounding structures, such as the neurovascular bundles, rectal wall, and bladder neck .Studies have shown the added value of T2-weighted MRI) in localising prostate carcinoma [35].

Conclusion

Multi parametric magnetic resonance imaging (mp-MRI) has better clinical role in diagnosis and management of prostrate carcinoma than a single parameter. However cost factor and availability is the limitation.

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