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RESEARCH ARTICLE

DIFFUSION WEIGHTED IMAGING IN PROSTATE CANCER A REVIEW.

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Abstract

Diffusion Weighed Imaging (DWI) is a sequence of specific Magnetic Resonance Imaging (MRI) and software generated images from the data which uses the diffusion of water molecules to generate contrast in Magnetic Resonance images. It allows to guide the diffusion of water molecules non-invasively, particularly in biological tissue in vivo. DWI is routinely used in MRI for the evaluation of prostate cancer. In this article, we review the general view of the Diffusion Weighted Imaging, its advantages over being used; and its limitations which can be developed into technique to improve the accuracy of Magnetic Resonance Imaging in prostate cancer. The correlation of Diffusion Weighted Imaging with b value and Gleason Score in prostate cancer for prognosis of the disease.

Introduction:-

Prostate Cancer(PC) is the most common malignant tumor among adult males and second cause of cancer related deaths after lung cancer.(1) In men, elevated serum PSA level and DRE leads to early detection of prostate cancer before transrectal ultrasound (TRUS) guided biopsy. Due to high false negative rate of invasive TRUS guided biopsy, mpMRI has been in practice for more accurate specificity and sensitivity for clinically significant prostate cancer.(2)

Multiparametric Magnetic Resonance Imaging (mpMRI) consists of anatomical (T1- and T2 weighted imaging [WI]) and functional MRI sequences such as diffusion-weighted imaging (DWI) and dynamic contrast-enhanced (DCE)-MRI. For PC, the recent advance in technology have reported that 3-T DWI have improved in diagnostic as well as for determining the location, size , and aggressiveness of the tumor which helps in staging, biopsy, post treatment follow-up and assessment of therapeutic response.(3,4)

Why DWI for prostate cancer?

For PC, MRI was previously performed with T2WI for the purpose of staging and organ confined PC or the extracapsular extension and seminal vesicle invasion.(5) Recently DWI MRI helps expand in diagnostic role of PC. T2 helps identifying prostate zonal anatomy and extracapsular integrity for PC diagnosis. T2 image along with DWI and other MRI modalities results in improvement of diagnostic performance of PC.(6)

The small part taken on the biopsies of the prostate cancer and the samples from the prostatectomy shows difference in the GSs. Therefore with the aid of DWI MRI with T1 and T2-WI, GS could be assumed preoperatively,

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intraoperative descision making regarding surgical margins and neurovascular bundle preservation and later to access the risk of PC recurrence and extent of malignancies.(7,8)

The literature reviewed that DWI along with T2WI increases both sensitivity and specificity in detecting PC.(9) This may be attributed to increased contrast on DWI images compared with conventional imaging. When combined with T2WI sensitivity of 71-89% and specificity of 61-91% which is higher than T2WI alone(sensitivity of 51-86% and specificity of 60-84%).(10–13) Lim et al. showed that combined T2WI and DWI imaging increased the AUC among readers from 0.66–0.79 for T2WI alone and 0.74–0.86 for DWI alone, to 0.76–0.9 ($p<0.001$).(14) DWI presently doesn't acheieve the same spatial resolution as T2WI, which is crucial for the assessment of extracapsular extension. Therefore, DWI at present should be combinedly used rather than replace T2WI.(9,15)

If mp-MRI is likely to become a screening tool on a larger scale for prostate cancer, the test should be short and cost efficient; likewise the mp-MRI protocol should be safe and the accuracy of the reports should be high among all the readers with different experience. Hoeks concluded in his article published on 2009 that mp-MRI was not appropriate for screening test due to its high cost and extent of availability.(16) It would have been cheaper if the protocol was made without the use of contrast. A protocol including T2WI, DWI (eg.0,50,400,800) for ADC calculation and an individual b2000 could reduce the scan time to less than 15min. Calculation of b2000 from low b value data set may yield similar performance to that of acquired DWI for lesion detection as well as to distinguish between intermediate, high and low grade prostate cancer and hence may further decrease examination cost.(17,18)

Gleason Score(GS):-

Gleason Score is a grading system which helps to evaluate the prognosis of men with prostate cancer using samples from prostate biopsy. The present standard at most of the institution is composed of taking 10-12 ultrasound guided transrectal biopsy samples of the prostate and computing specific Gleason grades to the cancerous tissue on the basis of the glandular patterns. The total of the primary grade (allocated to the dominant pattern of tumor) and the secondary grade (allocated to the next most frequent pattern) constitutes the cancer's Gleason score.(19,20) Combining with other parameters it is designed into a strategy of prostate cancer staging which predicts prognosis and helps guide therapy.

DWI has high detection rates especially in peripheral zone which is useful in evaluation of tumor aggressiveness(GS) and hence help identify clinically significant tumor for which therapy is needed. GS threshold ≤ 6 is one of the reason for the patient with PC to be kept under active surveillance therefore correct prediction is important to avoid underestimation of patient risk. Postoperatively 20-60% of patients with biopsy proven GS$\leq$6 are upgraded to GS$\geq$7.(21–25) There has been many investigation over preoperative clinical findings that may predict upgrading of GS. For GS upgrading serum PSA level, greatest percentage in cancer biopsy core, percentage of positive cores, clinical stage and the no. of TRUS-guided biopsy cores are the factors, however there are discrepancies among these studies with regard to variables used for prediction and biopsy schemes used(ie.6,8 or 12 cores).(22–24,26,27)

Bittencourt et al.and Yagci et al. showed that the findings of DWI MRI correlate well with GS from prostatectomy specimen rather than biopsy specimen.(6,8) In general prostatectomy is performed in localized or locally advanced PC. PC positive DWI MRI findings ($p=0.0059$) and a high GS (8 or more) ($p=0.0051$),was associated with locally advanced PC which suggests that DWI MRI has positive result for PC with high malignancy.(5)

Katsumi Shigemura et al. investigated the prediction of high GS in PC using DWI MRI. GS is correlated between tumor size or single or multiple tumor in DWI MRI findings. Patient with single tumor has higher GS as compared with patient with multiple tumor. This findings helps predict higher gleason score in correlation with single or multiple tumor correlated in GSs. The single tumor detected by DWI MRI tends to be larger and have higher malignant potential with high risk of tumor invasion than that of multiple tumor. He concluded that that prostatectomy was performed for locally advanced PC and locally advanced PC includes significantly higher ratio of PC-positive DWI MRI findings($p=0.0059$) and a high GS (8 or more) ($p=0.0051$), which suggests that PC-positive DWI MRI may reveal PC with a high malignant potential.(5)

Recently Sung et al. concluded that DWI may help predict GS upgrading in PCa with biopsy-proven GS ≤ 6. The variable ADCmin seems to perform better than ADCmean.(28)

B value in prostate cancer:-

There's still controversy on the optimal b-value to use in prostate DWI. Most researches and practices have used the b value of 0-1000 sec/mm2.(10,29) There is a need of standardization. However in few investigations of prostate DWI b value greater than1000 sec/mm2 has also been performed.(30–32) In prostate cancer, ADC values decrease when b values increase beyond 1,000 s/mm2. This can be explained by biexponential signal decay. Fast and slow diffusion components have been described in human brain models, and signal intensity is dominated by fast diffusion at relatively low b values, whereas at high b values, signal intensity is governed predominantly by slow diffusion.(33,34) According to a recent study, ADC maps using a high b value (2,000 s/mm2) showed little additional benefit over using the standard b value (1,000 s/mm2) in differentiating malignant from benign prostate tissue.(30). Recently Woo et.al performed a head to head comparision between high b value(>1000s/mm2) and standard b-value(800-100s/mm2)DWI regarding diagnostic performance in the detection of prostate cancer which concludes that high b value DWI has significantly better sensitivity and specificity in the detection of prostate cancer than standard b value. (35)

Lots of studies have demonstrated the association of apparent diffusion coefficient (ADCm) values, derived from DWI signal decay using the monoexponential model, and gleason score. Therefore, additional measurement of low b values for the calculation of ADC value still seems advisable. This should be done in different order, as prominent noise in b2000 can lead to calculation of falsely low ADC values. An accurate prediction in ADC values is particularly critical in active surveillance regimes for early detection of malignant transformation of formerly low grade tumors.(36)

DWI has a high detection rate for prostate cancer especially in the peripheral zone. Prostate cancer has a wide range of aggressiveness so accurate characterization and identification is needed in order to limit overtreatment while improving survival and quality of life. Histopathological evaluation of prostate cancer aggressiveness is one of the most significant prognostic aspects used in predicting patient outcomes and disease free survival. The final pathologically proven GS by means of TRUS guided biopsy is usually underestimated which is a well-known problem. A study done in 2001 confirmed that GS was underestimated in 46% and overestimated in 18% of cases. Well differentiated tumors maintain their tubular architecture whereas more cellular components dominate aggressive cancers. High cellular density leads to a restriction of the random motion of water molecules, an attribute that can be quantified with ADC values. A number of recently published articles have demonstrated an inverse correlation between the ADC and the final GS after prostatectomy.

Current Limitation and Future Directions:-

1. DWI is currently considered as an important component of prostate mpMRI examination, where it has been established as important sequence for detection of prostateCa.(37)
2. Recent methods of DWI MRI at 1.5 and 3 T has still limitations which are yet to overcome. Different institution have different methods which lacks the standardization. Various b values used in prostate DWI result in various ADC values in prostate cancer.(38,39)
3. These days prostate DWI has been used in clinical setting for the assessment of prostate cancer but fewer studies has been published about investigating its reproducibility.
4. DWI has an existing flows like imaging distortion and susceptibility artifacts which makes accessing the therapeutic response after hormonal and therapeutic therapy in prostate cancer challenging.therefore to overcome these problems more advanced software and hardware needs to be developed.
5. More in vivo studies are required to determine and elucidate the pathologic changes related to the features observed at DWI.(40)

Conclusion:-

Diffusion Weighted Imaging is a non invasive technique potential to detect qualitative and quantitative information about the tumor cellularity and tissue structure in prostate cancer. It is also useful in diagnostic therapeutic and post-treatment follow-up. However, optimization and standardization of parameters is necessary to boost up its potential.

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