International Journal of Research in Medical Sciences
Yadav P et al. Int J Res Med Sci. 2016 Nov;4(11):4877-4883
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20163784

Original Research Article

Role of multiparametric MRI in detection of prostatic lesions; of evaluation contrast enhanced MRI, diffusion weighted imaging and MR spectroscopy in malignant and benign prostatic lesions

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Received: 28 August 2016
Revised: 29 August 2016
Accepted: 29 September 2016

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ABSTRACT

Background: Prostate cancer is the most commonly diagnosed cancer in males and one of the leading causes of cancer-related death in men. Pretreatment assessment of prostate cancer is divided into detection, localization, and staging; accurate assessment is a prerequisite for optimal clinical management and therapy selection. The purpose of the study is to determine the diagnostic accuracy of multiparametric MRI for prostatic cancer detection using T2 weighted MR imaging, diffusion weighted imaging (DWI) and contrast enhanced MRI. To determine the use of MR spectroscopy in prostatic lesions.
Methods: It is a prospective single institutional study done on 29 patients with prostate lesions and elevated PSA level. Axial, coronal and sagittal images were obtained using T1WI, T2WI and STIR sequences. Advanced sequences like Diffusion weighted images, Spectroscopy and post gadolinium T1WI were taken after the basic MRI images.
Results: Study was done in 29 patients, age was ranging between 51years to 90 years, mean age is 70.7 years. On multiparametric MRI findings 45% were detected malignant lesions and 55% patients detected benign lesions. On biopsy correlation 42% of these cases turned out to be malignant and 58% as benign lesions. Detection of malignancy by T2WI imaging alone given sensitivity of 80.1% and specificity of 85.4%.By DWI alone sensitivity was 85.7% and specificity was 89.4%,on MRS sensitivity is 90.6% and specificity was 91.1%. Combined (MRI+DWI+MRS) gave sensitivity of 92.3% and specificity of 94.4% for detection of malignant prostatic lesion. Positive predictive value is 90% and negative predictive value was 88%.
Conclusions: The best characterization of prostatic cancer in individual patients will most likely result from a multiparametric exam. Recent advances include additional functional and physiologic MR imaging techniques (diffusion weighted imaging, MR spectroscopy, and perfusion imaging), which allow extension of the obtainable information beyond anatomic assessment. Multiparametric MR imaging provides the highest accuracy in diagnosis and staging of prostate cancer.

Keywords: Diffusion weighted, Magnetic resonance imaging, Multiparametric, Prostate cancer, Spectroscopy

INTRODUCTION

Prostate cancer is the most common cancer detected in men in the United States. Approximately 230,000 American men were diagnosed with prostate cancer in 2005.[1] Prostate cancer is the second leading cause of cancer death for men.

Despite the efficiency of clinical staging, it remains imperfect for precise local cancer staging and intra

prostatic tumor localization, both of which play important roles in initial assessment, treatment, and, in many cases, follow-up. Controversy exists with regard to the appropriate management of prostate cancer. The choice of treatment depends on the patient's age at diagnosis, the stage and aggressiveness of the tumor, the potential side effects of the treatment, and patient comorbidity.[2-4]

Magnetic resonance imaging (MRI) enable the noninvasive evaluation of anatomic and biologic tumor features and, thus, may play an important role in the detection, localization, and staging of prostate cancer and help guide treatment selection and planning.[5] Multiparametric MRI is MR examination using T1WI,T2WI & STIR in different planes and combining it with different functional studies e.g. dynamic contrast study, diffusion weighted and MR spectroscopy to differentiate benign and malignant prostatic lesion We can use pelvic coil For detection and localisation of lesion but for accurate staging endorectal coil should be used.

A recent study evaluating MRI in patients with elevated PSA and no previous biopsy found a higher cancer detection rate (30% vs 10%) and higher positive core biopsy rate (10.0% vs 2.5%) in the MRI group compared with the non-MRI group.[6] Because MRI is the most accurate imaging modality for localization of prostate cancer, MRI-guided prostate biopsy offers the possibility of more precise targeting.[7]

METHODS

The study was carried out on 29 patients in the department of Radio-diagnosis of the tertiary care university hospital over a period of 14 months after obtaining clearance form institution ethics committee. Patients having high suspicion of prostatic cancer were included in the study group. All MRI were done on high field strength MRI (1.5 Tesla Siemen's Avonto) using pelvic phased-array coils. Images were obtained using 256 x 256 matrix, 30 cm field of view, and 3 mm slice thickness. Axial, coronal and sagittal images were obtained using T1WI, T2WI and STIR sequences. After obtaining basic MRI images functional MRI using Diffusion weighted images, Spectroscopy and post gadolinium T1WI. The patients with metallic implants, cardiac pacemakers, claustrophobia and other conditions contraindicated for MRI were excluded from our study. Correlation with PSA levels was done. All the cases were correlated with the biopsy findings. Using PIRADS, patients were further classified for risk stratification. Data collected was analysed.

Imaging protocol

Sequences used – T1, T2, STIR, DWI with ADC, T1 contrast in multiple planes. MR spectroscopy also performed in three dimensional grids of multiple voxels.

Table 1: Imaging protocol.

Sequence	TE (ms)	TR (ms)	FOV (mm)	Slice Thickness (mm)
T1 (axial)	11	643	200	3
T2 (axial)	105	4000	200	3
T2 (sagittal)	107	3500	200	3
DWI	80	3700	260	3.6
T1 contrast	1.69	4.7	260	3.6

RESULTS

The study was done in 29 patients of prostatic lesions on MR imaging. Patients age was ranging between 51years to 90 years, mean age was 70.7 years. On multiparametric MRI findings 45% were detected malignant lesions and 55% patients detected benign lesions (Table 1).

Table 2: Table of the probable MRI diagnosis in prostatic lesions.

Probable diagnosis on MRI	Number of patients
Malignant	10
Probably Malignant	3
Benign	16

On biopsy correlation 42% of these cases turned out to be malignant and 58% as benign lesions (Table 2).

Table 3: Histopathology diagnosis of prostatic lesions.

Diagnosis on biopsy	Number of patients
Malignant	12
Benign	17

Detection of malignancy by T2WI imaging alone given sensitivity of 80.1% and specificity of 85.4%. By DWI alone sensitivity was 85.7% and specificity was 89.4%, on MRS sensitivity is 90.6% and specificity was 91.1%. Combined (MRI+DWI+MRS) gave sensitivity of 92.3%

and specificity of 94.4% for detection of malignant prostatic lesion (Table 3). Positive predictive value is 90% and Negative predictive value was 88%. The malignant lesions showed hypointense signal intensity (Figure 1a). Post gadolinium MRI showed heterogenous enhancement (Figure 1b). MRI is very useful to detect the pelvic lymph nodes in these patients (Figure 1b).

Table 4: Sensitivity and specificity of the individual MRI sequences and sensitivity and specificity of the combined (multiparametric) MRI in the prostatic lesions.

Sequence	Sensitivity	Specificity
T2WI	80.1	85.4
DWI	85.7	89.4
MRS	90.6	91.1
Overall (T2+DWI+MRS)	92.3	94.4

On magnetic resonance spectroscopy the malignant lesions showed increased choline level and decreased Citrate level (Figure 1c and d). The malignant lesions can show heterogeneous signal intensity on T2WI (Figure 2a). On post contrast MRI it showed heterogeneous enhancement (Figure 2b). On diffusion weighted images malignant lesions showed restriction with corresponding low ADC values (Figure 2 c and d). The benign lesions showed hyperintese signal intensity on T2WI (Figure 3a and b), did not show restriction on DWI and did not showed reduced ADC values (Figure 3c and d). On MRS benign lesions showed decreased choline level and normal citrate level (Figure e).

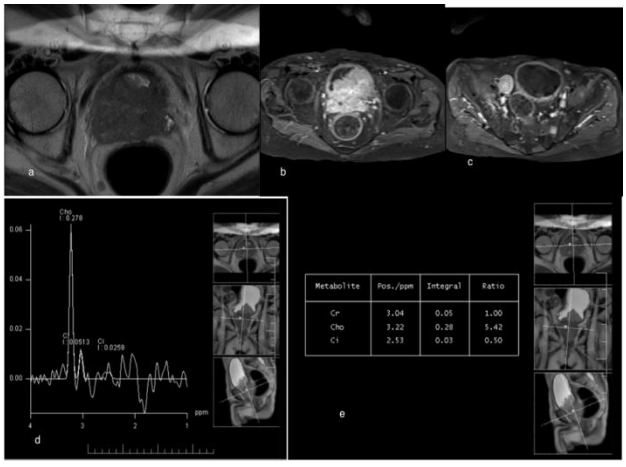

Figure 1: Carcinoma prostate in 62 years old patient; (a): axial T2WI showing loss of central and trannsition zone, enlarged gland, hyperintense signal intensity; (b): Axial T1 Fat sat Post contrast MRI showing intense heterogenous enhancement in the prostate mass; (c): Axial T1 Fat sat post contrast image showed enlarged lymph nodes in the pelvis; (d) and (e):MR spectroscopy of the lesion showed choline peak and significantly reduced citrate resonance.

Magnetic resonance imaging of prostatic lesions using multiparametric approach helps in diagnosing the cancer in all of the cases. It is very useful in characterization of lesion, staging and extent of disease to best determine diagnostic or treatment strategies, which range from biopsy guidance to active surveillance to radical prostatectomy.

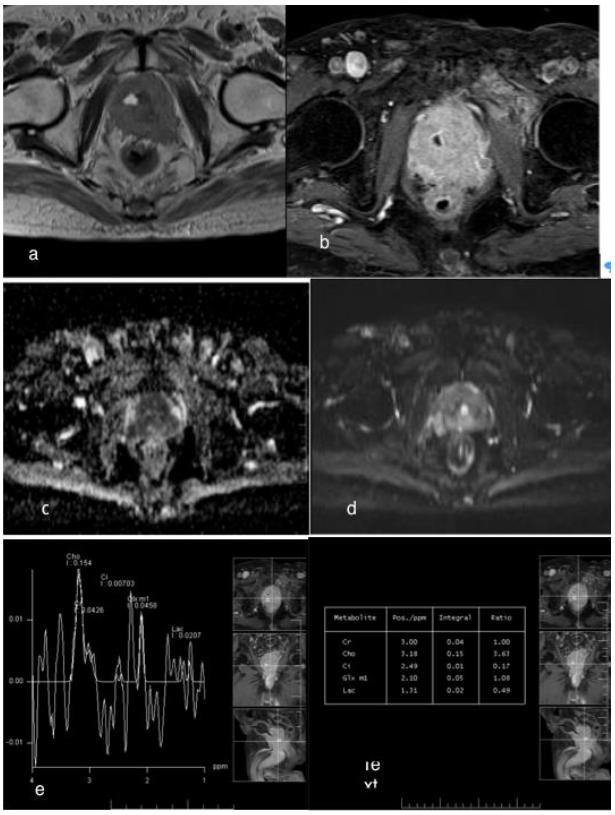

Figure 2: MRI of carcinoma prostate in 76 years old patient. (a): Axial T2WI showing heterogenous signal intensity lesion in the prostate; (b): Axial T1 Fat sat Post contrast MRI showing intense heterogenous enhancement in the prostate mass; (c):Axial DWI showing restriction; (d): The lesion is showing low ADC (e) & (f): Showing increased Choline and reduced citrate level.

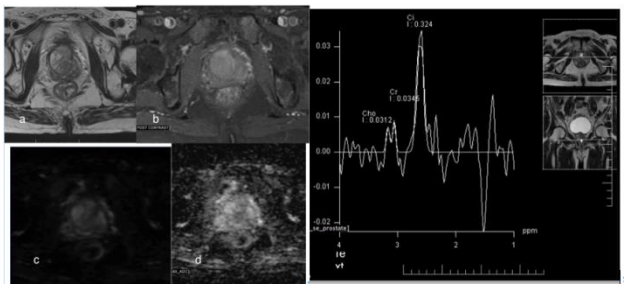

Figure 3: MRI of prostate in benign prostatic hypetrophy; (a): Axial T2WI showing hyperintense lesion involving prostate (b): Post contrast T1WI axial image showing enhancement (c) & (d): Axial DWI showing no restriction and ADC was high (e): MRS showing normal citrate and low Choline values.

DISCUSSION

T2-weighted MR imaging is the workhorse of prostate MR imaging. T2-weighted MR images have high spatial resolution and, thus, can clearly differentiate the normal intermediate- to high-signal-intensity peripheral zone from the low-signal-intensity central and transition zones in young male subjects.[8] In the aging man, owing to variable extension of the transition zone due to BPH, the size and signal intensity of the prostate transition zone may vary.

High spatial-resolution T2-weighted rapid acquisition, refocused echo sequences with a small field of view, performed with endorectal and/or external body phased-array coils, are generally used to depict prostate anatomy. T1-weighted contrast in the prostate is very low. Therefore, it is not possible to appreciate the different anatomic zones on T1-weighted images. On T2-weighted images, prostate cancer can appear as an area of low signal intensity within the high signal intensity of a normal peripheral zone.

The degree of signal intensity decrease may differ with the Gleason score: Higher Gleason score components 4 or 5 have shown lower signal intensities than do lower Gleason score components 2 and 3.[9] The density and the growth pattern of the cancer may also influence T2-weighted signal intensity. Cancers in the peripheral zone, which grow thinly scattered into the surrounding normal tissue, have shown no significant difference in quantitative T2 values with normal peripheral zone. On the other hand, densely growing cancers do show lower quantitative T2 values.[10]

A limitation of T2-weighted imaging is that focal areas of low signal intensity in the peripheral zone do not always represent cancer. Benign abnormalities such as chronic prostatitis, atrophy, scars, post irradiation or hormonal treatment effects, hyperplasia, and post biopsy hemorrhage may mimic tumor tissue.[11] Low-signal-intensity lesions with a wedge shape and a diffuse extension without mass may be reliable signs of benignity.[12] Hemorrhage may be differentiated on the basis of its high signal intensity on T1-weighted images. When methemoglobin is present in hemorrhagic regions, its paramagnetic characteristics result in high signal intensity on T1-weighted MR images.

Preferably, MR imaging of patients suspected of having prostate cancer should be avoided for 8 weeks after prostate biopsy to allow reduction of artifacts due to post-biopsy hemorrhage.[13] Owing to the presence of BPH, cancer in central and transition zones is more difficult to discern. BPH may have signal intensity similar to that of prostate cancer on T2-weighted images. However, it has been reported that features such as homogeneously low T2-weighted signal intensity, ill-defined irregular edges of the suspicious lesion, invasion into the urethra or the anterior fibromuscular stroma, and lenticular shape are helpful signs for detection of malignancy in the transition zone.[14] Combined T1-weighted and T2-weighted MR imaging should be used for all clinical prostate cancer indications to evaluate anatomy and possible post-biopsy hematoma artifacts.

Angiogenesis in prostate cancer tissue is induced by secretion of vascular growth factors in reaction to the presence of local hypoxia or lack of nutrients.[15] Resultant changes in vascular characteristics can be studied well with contrast-enhanced MR imaging. This technique exploits the uptake and rapid washout of a gadolinium chelate contrast agent to show the typical pharmacokinetics of cancerous tissue. Because the prostate as a whole is highly vascularized, a simple comparison of pre- and post-gadolinium images is usually insufficient to discern prostate cancer.[16,17]

A fast and direct method to characterize prostatic vascular pharmacokinetic features is high-temporal-resolution contrast-enhanced MR imaging. Dynamic contrast-enhanced MR imaging consists of a series of fast T1-weighted sequences covering the entire prostate before and after rapid injection (2–4 mL/sec) of a bolus of a low molecular- weight gadolinium chelate such as gadoterate meglumine or gadopentetate dimeglumine (concentration, 0.1–0.2 mmol/kg).[18,19] In addition to the most frequently used fast sequences, which have a high temporal resolution (a short period of 1–4 seconds between measurements), slow sequences (temporal resolution, 30 seconds with higher spatial resolution) have also been used.

Depending on the area of anatomic coverage, the acquisition times, potential susceptibility artifacts, and desired T1 sensitivity, a choice for a faster or slower sequence must be made.[20] On one hand, fast sequences may improve tissue characterization because the prostate enhances quickly with T1-weighted contrast-enhanced MR sequences. With fast sequences, accurate quantification of different pharmacokinetic enhancement parameters is possible. On the other hand, fast T1-weighted sequences have trade-offs, including reduced spatial resolution and/or anatomic coverage. Optimal spatial and temporal resolutions based on clinical indications remain subjects of future research.

Assessment of signal intensity changes on T1-weighted dynamic contrast-enhanced MR images in order to estimate contrast agent uptake in vivo can be performed qualitatively, semi quantitatively or quantitatively. Prostate cancer tends to enhance earlier, faster, and to a greater extent and shows earlier contrast agent washout, as compared with healthy prostate tissue.[18,21] This characteristic makes contrast-enhanced MR imaging a sensitive technique for prostate cancer localization. Prostate cancer diagnostics for clinical indications such as local staging can then be improved by better prostate cancer localization characteristics obtained with contrast enhanced MR imaging. One of the limitations of contrast-

enhanced MR imaging is related to discrimination of cancer from prostatitis in the peripheral zone and from highly vascularized BPH nodules in the transition zone.[22] Other shortcomings are a limited use of standardized approaches for calibration and analysis, the shortage of uniform commercially available tools for pharma-cokinetic analysis, and the lack of consensus in acquisition protocols. In multiparametric MR imaging examination, the high sensitivity of dynamic contrast-enhanced MR may be used for initial evaluation of potential tumor locations.

In DW imaging, proton diffusion properties in water are used to produce image contrast. Images that reflect proton diffusion are acquired by applying motion encoding gradients, which cause phase shifts in moving protons, depending on the direction and quantity of their movement.[23] The attenuation of the MR signal in DW imaging is expressed with the Stejskal-Tanner equation.[23]

The b value and the apparent diffusion coefficient (ADC) are components in this equation. While the b value expresses the amount of diffusion weighting, ADC reflects the movement of the water molecules within the inter pulse time. Because ADC quantifies the flow as well as the distance a water molecule has moved, it represents both capillary perfusion and diffusion characteristics.[24] For prostate cancer, DW imaging b values between 500 and 800 sec/mm 2 are typically used.[25] b Values of 1000 and even 2000 sec/mm 2 may increase the accuracy of prostate cancer detection.[26]

Especially within the transition zone, high b values may help improve differentiation of BPH from prostate cancer.[27] Healthy prostate tissue in the peripheral zone, which is rich in tubular structures, allows extensive diffusion of water molecules within the gland tubules. Consequently, ADCs in healthy peripheral zone tissues can be high. Prostate cancer tissue destroys the normal glandular structure of the prostate and replaces ducts. It also has a higher cellular density than does healthy prostate peripheral zone tissue.[25]

On ADC maps, therefore, prostate cancer often shows lower ADCs in comparison to surrounding healthy peripheral zone prostate tissue.[28] Because the acquired ADC depend on the specific pulse sequence parameters (especially the b values), the specific MR systems used, and the magnetic field strength, the ADCs of healthy and cancerous tissue have varied among reported studies.

Furthermore, there is an overlap in the ADCs of healthy tissue and those of prostate cancer, within and between subjects, which limits the determination of a single threshold ADC for malignancy.[29] DW imaging is a fast, simple, and readily available MR imaging technique for prostate cancer. Nevertheless, DW imaging of the prostate has the limitation of low in-plane spatial resolution, even at 3 T. Consequently, DW imaging is not a preferred technique for prostate cancer staging. However, DW imaging does reflect cellular density, which makes the technique potentially suitable to determine tumor aggressiveness. DW imaging, being a technique for measuring proton motion, is very sensitive to motion artifacts. Single shot echo-planar MR imaging is used to decrease motion artifacts by acquiring images in less than 1 second.

Because the phase-encoding bandwidth per pixel is very small, echo-planar imaging is very sensitive to magnetic field inhomogeneity. As a result, artifacts occur in areas with large variations in magnetic susceptibility, such as in tissue-air interfaces (air in the rectum or endorectal coil) or in chemical shift in areas with water-fat interfaces. Parallel imaging and short-imaging-time protocols are used to overcome these off-resonance artifacts.[30] Of all functional MR imaging techniques DW imaging is the most practical and simple in its use. DW imaging has the disadvantages of being susceptible to motion and to magnetic field inhomogeneity.

In MR spectroscopic imaging, spectral profiles are measured in two or three spatial dimensions. These spectral profiles reflect resonance frequencies that are unique for protons in different metabolites present at the sampled location. The specific resonance frequencies or chemical shifts are given relative to a reference frequency in parts per million (ppm). In human prostate examinations, MR spectroscopic imaging is usually performed in a volume that covers the whole prostate, which is subdivided up into a three-dimensional grid of multiple voxels.

The dominant peaks observed in these spectra are from protons in citrate (approximately 2.60 ppm), creatine (3.04 ppm) and choline compounds (approximately 3.20 ppm). Polyamine signals (mostly from spermine) also may be observed (approximately 3.15 ppm) at various relative intensities, depending on the acquisition conditions. Compared with healthy peripheral tissue or BPH tissue, citrate signals are reduced and those of choline compounds are often increased in prostate cancer tissue.[31] Citrate is produced in epithelial cells as an intermediate product in the Krebs cycle due to aconitase inhibition.

It then accumulates in the luminal space of the prostate. The lower citrate peak in cancer tissue may thus be caused by altered metabolism, as well as by a reduction of luminal space, which commonly occur in prostate cancer. Choline compounds are involved in the biosynthesis and degradation of phospholipids, which are required for the build-up and maintenance of cell membranes.

An increased cell-turnover in prostate cancer results in an increased concentration of free choline-containing molecules within the cytosol and the prostate interstitial tissue. Because differentiation of choline peaks from creatine peaks on spectra obtained at common clinical

field strengths is often hampered by their bandwidths and by weaker signals from polyamines between them, the choline plus creatine–to-citrate ratio is mostly used as a metabolic biomarker for prostate cancer. In the analysis of patient data, it should be taken into account that different anatomic zones of the healthy prostate have different amplitudes for citrate, creatine, and choline, which are reflected in different choline plus creatine–to-citrate ratios.

High citrate concentrations are found in the glandular tissues of the prostate such as the peripheral zone, which contains epithelial cells and secretory ducts. Therefore, citrate concentrations are highest in the peripheral zone and lower in the central zone. In the transition zone, the citrate concentration may be higher in case of glandular proliferation and lower in the case of stromal proliferation.[32] Three-dimensional MR spectroscopic imaging sequences are currently preferred over two-dimensional sequences because of the possibility of complete coverage of the entire prostate gland.[33,34] Three-dimensional acquisitions can be performed in approximately 10–15 minutes with a resolution as low as 0.4 cm 3 with sufficient signal-to-noise ratio at 1.5 T.[33] MR spectroscopic imaging has several limitations. Spectral quality depends on magnetic field homogeneity, which must be optimized for each patient by shimming. Considerable local magnetic field distortions may occur due to hemorrhage, which is why the examination should be performed with sufficient delay from the time of biopsy. The clinical performance of MR spectroscopic imaging of the prostate can be improved by optimizing field shimming or by means of correction procedures, in addition to better signal-to-noise ratio and chemical shift dispersion, by using stronger magnetic fields.[35] Currently, the interpretation of MR spectroscopic imaging results requires special expertise and is time consuming. Automated measurement procedures, rapid display of examination results, and proper training of clinical users are important to transform MR spectroscopic imaging into a practical and widespread clinical tool.

CONCLUSION

To this day, these requirements are generally not met. MR spectroscopic imaging is an accurate technique that may be used for all clinical indications mentioned in this article. However MR spectroscopic imaging needs relatively more time and expertise than do other functional MR imaging techniques, which limits its clinical applicability.

Clinical application

MR evaluation of prostate is an excellent noninvasive investigation to differentiate malignant from benign pathologies. Best characterisation of the prostatic lesions result from multiparametric MRI which includes DWI and MR spectroscopy. It help to reduce the number of biopsies in patients.MR imaging gives excellent tumor localization and staging of disease which is helpful in planning of surgeries and post treatment follow up.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Yadav P, Bhargava R. Role of multiparametric MRI in detection of prostatic lesions; evaluation of contrast enhanced MRI, diffusion weighted imaging and MR spectroscopy in malignant and benign prostatic lesions. Int J Res Med Sci 2016;4:4877-83.