Visualisation of periprostatic neurovascular bundles before and after radical prostatectomy by means of diffusion tensor imaging (DTI), with clinical correlations

Award: Cum Laude
Poster No.: C-2924
Congress: ECR 2017
Type: Scientific Exhibit
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Keywords: Pelvis, Genital / Reproductive system male, MR, MR-Diffusion/Perfusion, Diagnostic procedure, Computer Applications-Detection, diagnosis, Neoplasia
DOI: 10.1594/ecr2017/C-2924

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Aims and objectives

Prostate cancer is the most common malignant neoplasm in males, accounting for the 25% of all tumors and it is the second cause of death due to cancer. There are many treatments for the prostatic cancer such as hormone therapy and radiotherapy, but the treatment of choice of locally advanced and aggressive form of prostatic cancer is represented by radical prostatectomy (RP). Unfortunately this major surgery is related to some complications such as urinary incontinence and erectile dysfunction that reduce patient's quality of life. In order to avoid these complications new surgical techniques has been introduced, for example "nerve-sparing" laparoscopic, robot -assisted or intrafascial prostatectomy [1].

Magnetic Resonance Imaging (MRI) is the recommended imaging modality for patients with prostate cancer, and it is clinically indicated for diagnosis, staging and follow-up [2]. Diffusion tensor imaging (DTI) is a new MRI modality born in the field of neuroimaging which has emerged as noninvasive technique providing in vivo a successful depiction of central and peripheral nervous fibers [3-13]. This technique has been used for the neurosurgical planning in the removal of brain tumors [5] as well as for the depiction of neural pathway in the mapping of the brain, spinal cord and brachial plexus [13]. More recently DTI has been introduced as useful imaging modality in the mapping of the periprostatic fat tissue (PNF) [14-16].

The aim of this study is to evaluate if DTI is able to detect changes of periprostatic neurovascular bundles (pNVB) before and after radical prostatectomy (RP) and if these changes are related to post-surgical complications, such as urinary incontinence and erectile dysfunction.
Methods and materials

Twenty-five patients (mean age 64.8ys) with biopsy-proven prostate cancer underwent MRI including DTI sequence before and after RP between February 2014 and August 2016.

All DTI exams were performed on a 1.5-T MR unit (Ingenia; Philips Medical Systems, Eindhoven, Netherlands) using a multichannel phased array (16 + 16 channel coil) for signal reception.

Peristalsis was suppressed by intramuscular administration of 20 mg of scopolamine.

Before to start examination, patients were asked to have half-filled bladder to limit involuntary movements.

The dynamic imaging was performed during gadolinium chelate injection (0.1 mmol/kilogram of body weight gadolinium chelates MultiHance®, Bracco Imaging, Milan, Italy).

To our standard MRI protocol for the study of the prostate (shown in Table I) we added the Diffusion Tensor Imaging sequence which was acquired in 32 directions (TR/TE 1449/88 msec, thickness 3 mm, b value= 0, 800 s/mm^2). The scan duration for DTI sequence was 3’14”.

Images were independently analyzed by two radiologists placing six ROIs respectively at base, mid gland and apex, one for each side, before prostatectomy (Fig 1) in order to obtain Tractographic reconstruction of the fibers. After prostatectomy ROIs of the same size were placed in a similar plane of the empty prostatic loggia (Fig 2).

For each fiber tract the software evaluate the changes of the following 3 parameters before and after RP:

- number of fibers
- mean Fractional Anisotropy (FA) values
- mean length.

To investigate urinary continence and erectile function at each MRI, patients were asked to fill ICIQ-SF and IIEF-5 questionnaires.

Fractional anisotropy(FA), number and length of fibers for each ROI before and after RP were compared by means using T-Test. Spearman Test was used to evaluate correlation between DTI parameters and questionnaires scores before-after RP.
To investigate the clinical parameters each patient was asked to fill out two questionnaires before and after RP, one for the evaluation of urinary continence (ICIQ-SF) [17] and one for the evaluation of erectile function (IIEF-5) [18].

For the statistical analysis we used:

- **Interobserver agreement** for number, FA values and length of the fiber tracts before and after RP. It was assessed by means of intraclass correlation coefficient (ICC): < 0.20 poor agreement; 0.21-0.40 fair agreement; 0.41-0.60 moderate agreement; 0.61-0.80 good agreement; 0.81-1.00 excellent agreement.

- **Ratio** between numbers, the FA values and the length of the fiber tracts before and after RP for base, mid gland and apex (DTI B-A RATIOS).

- **Ratio** between scores before and after RP for (ICIQ-SF B-A RATIOS and IIEF-2 B-A RATIOS).

- **Student’s t-test** to evaluate if there were differences between numbers, FA, length of the fiber tracts before and after RP.

- **Spearman Test** to evaluate correlation between the DTI B-A RATIOS of: total number, FA and length of the fiber tracts; and the Scores B-A RATIOS: ICIQ, IIEF-2.
Table 1: MRI protocol for the study of the prostate.

<table>
<thead>
<tr>
<th>Pulse Sequence</th>
<th>Plane</th>
<th>TR/TE (ms)</th>
<th>Thickness (mm)</th>
<th>FOV (mm)</th>
<th>Flip angle</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>T2 TSE</td>
<td>Axial</td>
<td>4100/100</td>
<td>4</td>
<td>380x340</td>
<td>90°</td>
<td>1'30&quot;</td>
</tr>
<tr>
<td>T2 TSE (HR)</td>
<td>Sagittal</td>
<td>2650/90</td>
<td>3.5</td>
<td>200x200</td>
<td>90°</td>
<td>1'40&quot;</td>
</tr>
<tr>
<td>T2 TSE (HR)</td>
<td>Coronal</td>
<td>2500/100</td>
<td>3.5</td>
<td>160x160</td>
<td>90°</td>
<td>3'25&quot;</td>
</tr>
<tr>
<td>T2 TSE (HR)</td>
<td>Axial</td>
<td>3730/90</td>
<td>3.5</td>
<td>160x160</td>
<td>90°</td>
<td>4'10&quot;</td>
</tr>
<tr>
<td>DWI</td>
<td>Axial</td>
<td>4000/90</td>
<td>3.5</td>
<td>300x300</td>
<td>90°</td>
<td>7'47&quot;</td>
</tr>
<tr>
<td>DTI</td>
<td>Axial</td>
<td>1449/88</td>
<td>3</td>
<td>220x220</td>
<td>90°</td>
<td>3'14&quot;</td>
</tr>
<tr>
<td>T1 DIXON (mDC)</td>
<td>Axial</td>
<td>4/2</td>
<td>3.5</td>
<td>200x220</td>
<td>10°</td>
<td>3'17&quot;</td>
</tr>
<tr>
<td>b-SSFP</td>
<td>Axial</td>
<td>5000/80</td>
<td>6</td>
<td>400x350</td>
<td>90°</td>
<td>51'</td>
</tr>
</tbody>
</table>

Fig. 1: ROI in the periprostatic fat tissue before radical prostatectomy: base (A), mid gland (B) and apex (C).
Fig. 2: ROI in the periprostatic fat tissue after radical prostatectomy: base (A), mid gland (B) and apex (C).

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Results

NUMBER OF FIBERS BEFORE AND AFTER RP

The mean values of the numbers of fiber tracts before and after RP at base, mid gland, and apex levels for right and left side are reported in Table II and in the associated Graphic. The number of fiber tracts decreased after RP at base, mid gland, and apex for both right and left sides; the decrease was statistically significant for all these sites (p<0.01) (Fig. 3).

LENGTH OF FIBERS BEFORE AND AFTER RP

The mean values of the length tracts before and after RP at base, mid gland, and apex levels for right and left sides are reported in Table III and in the associated Graphic. The length of the fiber tracts does not change significantly after RP. This probably indicates that the residual fibers are not reduced in length (Fig. 4)

FRACTIONAL ANISOTROPY OF FIBERS BEFORE AND AFTER RP

The mean values of the fractional anisotropy tracts before and after RP at base, mid gland, and apex levels for right and left sides are reported in Table IV and in the associated Graphic.

The FA values at mid gland showed a decrease after RP (p<0.05) (Fig.5). No statistically significant differences were found for the FA values at base and apex. This may indicate that the fibers after RP are less oriented and more disarranged, analogously to other published studies which have demonstrated a decrease of the FA values in several neurological diseases, such as multiple sclerosis, astrocytic tumors and hypoxic ischemia.

CORRELATION OF DTI PARAMETERS WITH CLINICAL SCORE

Correlation between the DTI parameter ratio of: total number, FA and length of the fiber tracts; and the clinical score ratio for ICIQ, IIEF-2 are reported in are reported in Table V and in the associated Graphic.

There was a statistically significant correlation between the decrease of the number of fiber tracts and the decrease of erectile function after RP (p<0.05), suggesting that this decrease may have a role in the post-surgical erectile dysfunction.
No correlation were found with urinary incontinence. These results suggest that other factors in addition to neurovascular damage may concur to post-RP incontinence, such as the damage of the urethral sphincter during the apical dissection and the urethral length post-RP.

**INTEROBSERVER AGREEMENT**

Interobserver agreement values before and after RP for each parameter were good or excellent.
Table 2: Table and Graph: number of fiber tracts before and after RP.

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Fig. 3: Number of fiber tracts at base (A), mid gland (B) and apex (C) before radical prostatectomy. They were significantly lower (P<0.01) after radical prostatectomy at base (D), mid gland (E) and apex (F).
Table 3: Table and Graph: length of fiber tracts before and after RP.
**Fig. 4**: Tractographic reconstruction in the periprostatic fat tissue on the axial T2 images fused with the registered DTI images at mid gland on para-axial (A), coronal (B), sagittal (C) plane before RP and para-axial (D), coronal (E), sagittal (F) plane after RP. The length of the fiber tracts did not change significantly after RP: before and after RP the console reconstructed fibers of considerable length (arrow in B, C, E, F).

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Table 4: Table and Graph: fractional anisotropy tracts before and after RP

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**Fig. 5:** Tractographic reconstruction in the periprostatic fat tissue on the axial T2 images fused with the registered DTI images at mid gland on axial plane before and after RP. As shown on the screenshot of the reconstruction console, there is a decrease of the FA value after RP suggesting that the fibers after RP are less orientated and more disarranged.

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<table>
<thead>
<tr>
<th></th>
<th>DTI B-A RATIO ICIQ</th>
<th>DTI B-A RATIO IIEF-2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DTI B-A RATIO NUMBER</strong></td>
<td>N.S.</td>
<td><strong>p&lt;0.05, p=0.47</strong></td>
</tr>
<tr>
<td><strong>DTI B-A RATIO FA values</strong></td>
<td>N.S.</td>
<td>N.S.</td>
</tr>
<tr>
<td><strong>DTI B-A RATIO Length</strong></td>
<td>N.S.</td>
<td>N.S.</td>
</tr>
</tbody>
</table>

**Table 5:** Table and Graph: Correlation between the DTI parameter and the clinical scores ratio’s before and after RP.

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Conclusion

Diffusion Tensor Imaging (DTI) of the periprostatic neurovascular fibers (PNFs) has demonstrated to be a useful technique to detect a statically significant decrease of the number (p<0.01) and of the FA values (p<0.05) of the PNFs after Radical Prostatectomy.

The decrease of the number of the PNFs resulted statistically related to the decrease of post-surgical erectile dysfunction (p<0.05), suggesting that it could be an important factor related to the post-surgical erectile dysfunction and a potential good and reproducible technique to evaluate RP functional outcome.

The interobserver agreement was good - excellent, suggesting that the tractography of periprostatic neurovascular bundles is a feasible and reproducible technique, with fast learning curve, even if the agreement was slightly lower after RP; this was probably due to the loss of anatomic landmarks induced by surgery.
References


