Value of DTI parameters to differentiate prostate cancer in central gland from benign prostate hyperplasia

<table>
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<th>Poster No.:</th>
<th>C-0129</th>
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<tr>
<td>Congress:</td>
<td>ECR 2014</td>
</tr>
<tr>
<td>Type:</td>
<td>Scientific Exhibit</td>
</tr>
<tr>
<td>Authors:</td>
<td>T. GONG; Shandong Province/CN</td>
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<tr>
<td>Keywords:</td>
<td>Pelvis, Anatomy, CNS, Cone beam CT, Conventional radiography, CT-Quantitative, Biopsy, Balloon occlusion, Arthrography, Blood, Cavitation, Cerebral palsy</td>
</tr>
<tr>
<td>DOI:</td>
<td>10.1594/ecr2014/C-0129</td>
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Aims and objectives

According to global cancer statistics in 2011, Prostate cancer (PCa) is the second most frequently diagnosed cancer and the sixth leading cause of cancer death in men [1]. Among all prostate cancers, Central gland (CG) carcinoma composes about 30 percent [2]. Magnetic resonance imaging (MRI) has excellent soft tissue contrast but conventional MRI is difficult to differentiate CG cancer from benign prostate hyperplasia (BPH), because dysplastic nodules of prostate especially stromal hyperplasia (SH) foci is hypo-intense on T2-weighted images which mimic CG cancer. Diffusion tensor imaging (DTI) is a common noninvasive method of measuring the apparent diffusion coefficient (ADC) and fractional anisotropy (FA) of water diffusion, which may reflect physiological features and pathological changes [3]. Recently, a number of studies have shown that ADC value obtained from Diffusion Weighted imaging (DWI) can improve the differentiation of CG cancer from BPH [4-8]. There were also a few studies reported the potential of prostate Diffusion tensor tractography (DTT) in evaluating the microstructural organization of the prostate [9-10]. To the best of our knowledge, there have as yet been no studies into differentiating CG cancer from BPH using DTI and DTT. So the purpose of our study was to evaluate the ability of DTI related parameters ADC, FA value and DTT map to different the CG cancer from BPH.
Methods and materials

Study population

This retrospective study was conducted with an Institutional Review Board-approved waiver of informed consent. We searched patients up to standard in our institution for patients who underwent 3T prostate routine MRI and DTI, between February 2013 and November 2013, 46 patients complied with the standard set, 16 cases of CG cancer (average age, 65.5 years; range 45~81 years) proven by histopathologically. 19 BPH (average age, 66.0 years; range, 41~78 years) underwent pathological examination, and proven. Other 11 BPH had no pathological result, the follow-up stability of at least 6 months was considered benign.

MRI protocol

All MRI examinations were performed with American skyra 3.0 T scanner (Siemens, Germany) using a 8 channel phased-array coil with abdominal circle as the receiver coil. The study use the scope for the center with prostate, line integral imaging of prostate, supine position, sequence composed of conventional axial T1WI, T2WI, FS - T2WI, sagittal and coronal T2WI and other conventional MRI sequences and DTI sequence. The DTI imaging using single excitation spin echo imaging plane (SE - EPI) cross-sectional imaging, parameters: TR 4900 ms; TE 75 ms; FOV 26 cm, slice thickness 3.0 mm; inter-slice gap 1 mm; 6 direction of diffusion sensitive gradient; b values 0 and 800 s/mm$^2$. DTI image acquisition time was 7 minutes 6 seconds.

Data analysis

After data acquisition, all images were transferred to Siemens post-processing workstation, via Neuro3D post-processing software to generate the ADC and FA map, using axial T2-weighted images as anatomical guide and ROIs were drawn on it. CG cancer group according to pathological results and abnormal signals of the image of T2WI images, ROIs as far as possible includes the entire lesion, but not exceed the area of lesions. The average ADC within each ROI was then calculated as the final ADC and FA value. As for BPH group, ROIs were drawn on the level containing the most dysplastic nodules, especially SH foci.

And then tracking its fibers with seed point method, covers the entire area of the CG gland and peripheral zone in the same level of lesion above, generate DTT map. Anisotropy was selected 2.0, and angular was 45 degree. Different color represented different orientation of diffusion: blue, craniocaudal direction; red, right-left; green, antero-posterior. Date analysis was performed by two radiologists. Each observer recorded the score using a four-point scale: 1, the fibers run orderly, continuously and arrange closely; 2, the fibers was less orderly and continuous than point 1; 3, the fibers was disorder and poor
continuity; 4, the fibers was very disorderly, discontinuous and loosely arranged. Figure out the score of DTT map obtained from CG cancer and BPH, and compare whether there is a difference between two groups.

Statistical analysis using Student's t-test, \( P < 0.05 \) was regarded as statistically significant. SPSS 19.0 statistics software was used to perform all statistical calculations. Additionally, interobserver agreement on the scale for each image interpretation sessions was analysed.
Images for this section:

**Fig. 1:** a. The green color represent seed points covering the whole prostate in the level to track the fibers, and then get the b, c, d map. b. axial DTT map. c. coronal DTT map. d. sagittal DTT map. The fibers was disorder and poor continuity (rated 3 on four-point scale)

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Results

60 ROIs were defined, 20 were CG carcinoma, and 40 were hyperplasia foci. ADC value and FA value in BPH-PCa tissues were: $(1357 \pm 163) \times 10^{-6} - (1058 \pm 196) \times 10^{-6} \text{mm}^2/\text{s}$, and $(356 \pm 116) \times 10^{-3} - (407 \pm 132) \times 10^{-3}$ respectively. ADC value between the two groups was statistically significant difference ($p < 0.05$). While FA values between the two groups have no statistically significant difference ($p > 0.05$). (table 1)

Interobserver agreement regarding the scale was good ($k = 0.723$). The two viewers' DTT map score of CG cancer were $2.9 \pm 0.9; 2.8 \pm 1.0$, the BPH were $1.8 \pm 0.7; 1.7 \pm 0.8$. The DTT map score between the two groups for two viewers were all statistically significant difference ($p < 0.05$). The result indicates that fibers of CG cancer are more likely to rupture, and loosely arranged in disorder compared with BPH. (table 2)
**Fig. 2:** A 70 years old patient with BPH, PSA: 5.46 ng/ml. a. Axial FS-T2 weighted MRI. b. ADC map. c. FA map. d. DTT map. The FS-T2 weighted MRI and ADC map showed multiple hypointense lesions in CG zone. DTT map demonstrate that fibers run orderly, continuously and arrange closely (rated 1 on four-point scale)

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**Fig. 3:** A 71 years old patient with biopsy-confirmed prostate cancer, a PSA level of 11.78 ng/mL. a. Axial FS-T2 weighted MRI. b. ADC map. c. FA map. d. DTT map. The FS-T2 weighted MRI and ADC map showed multiple apparent hypo-intense lesions in CG zone. DTT map demonstrate that fibers were very disorderly, discontinuous and loosely arranged. (rated 4 on four-point scale)

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<tr>
<th>Group</th>
<th>Number</th>
<th>ADC value ($\times 10^{-6}$ mm$^2$/s)</th>
<th>FA value ($\times 10^{-3}$)</th>
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<tr>
<td>CG cancer</td>
<td>16</td>
<td>1058±196</td>
<td>407±132</td>
</tr>
<tr>
<td>CG BPH</td>
<td>30</td>
<td>1357±163</td>
<td>356±116</td>
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**Table 1:** the ADC and FA value of CG cancer and BPH

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<table>
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<tr>
<th>Group</th>
<th>Number</th>
<th>DTT map score (viewer 1)</th>
<th>DTT map score (viewer 2)</th>
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<tr>
<td>CG cancer</td>
<td>16</td>
<td>2.9±0.9</td>
<td>2.8±1.0</td>
</tr>
<tr>
<td>CG BPH</td>
<td>30</td>
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**Table 2:** the DTT map score of CG cancer and BPH

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Conclusion

DTI is a powerful noninvasive imaging method to provide valuable data about the microstructure and histological properties of tissues which influence diffusion of water molecules. The application of DTI mainly focus on neuro- and musculoskeletal imaging [11-14]. With the advent of 3T magnetic field system and phased-array coils with parallel imaging technology, DTI has been used for abdominal organs, such as prostate. But conventional MRI is generally considered inadequate for differentiating CG cancer from BPH, because both of them could demonstrate hypointense on T2 weighted imaging. As is known to us all, the benign CG is composed of two histologically distinct types of issue: Glandular tissue and stromal tissue, so the hyperplasia foci contains SH and glandular hyperplasia (GH). The stromal tissue shows hypointense on T2 weighted imaging mimic CG carcinoma. So in our study, we chose the SH foci and hyperplasia foci comprising SH mostly as the matched group.

Our result show that DTI related ADC value of CG carcinoma decreases markedly compared with hyperplasia foci, which makes ADC value differentiate CG cancer from BPH significantly. Although FA value alone could not effectively distinguish CG cancer with BPH, the DTT map present different between them. Combining the DTT map with ADC value shows the possibility of improving this differentiation compared with ADC value alone.

ADC value is smaller in CG cancer than BPH, which owing to CG carcinoma is more cellular, more dense, and less extracellular fluid than hyperplasia nodules. Oto A et al [15] demonstrated CG cancer with smaller ADC values (1.05 ×10^{-3} \text{ mm}^2/\text{s}) compared with GH (1.73×10^{-3} \text{ mm}^2/\text{s}) and SH (1.27×10^{-3} \text{ mm}^2/\text{s}), which is concordant with our result. Some other studies also confirm the result similar to ours, but the ADC values all obtained by DWI. To date, there were no correlational studies above using DTI. Our results indicate that, despite some overlap between the ADC values of CG cancer and those of hyperplasia nodules, the ADC can help differentiate CG cancer from BPH.

Diffusion tensor tractography (DTT) imaging is currently the only method display the fibers bundle in living tissue. A few investigations have assessed tractorgraphy using DTI date of prostate, but they all relate to peripheral of prostate or nerve fibers around prostate [16-18]. The CG contains compact and organized smooth muscles fibers which make water molecules in the direction along the fibers bundle diffusion limited the smallest, diffusion fastest, show the anisotropic diffusion. In CG cancer, the carcinoma will push the fibers bundle and show the arrangement of the bundle disorderly, and destruct fibers bundle because of tumor infiltration and performance interruption of fibers bundle. In BPH hyperplasia, especially of fibrous tissue hyperplasia, DTT map visible fibers bundles are arranged in dense, otherwise because of hyperplastic nodule will also push fibers, making
it transposition orderly, and severe interruption phenomenon of fibers bundle would not be seen.

There are several limitations in our study. The first one is only a limited number of subjects were enrolled into our study, a large number will be put into this study. The second one is the use of pelvic phased array coil rather than endorectal coil, the latter is not available in our institution. The third one, it was difficult to correlation the MR image with the histological result accurately, and the CG cancer can be easily missed by biopsy due to limited needle length.

In summary, our study results suggest that the ADC value obtained by DTI and DTT map has the potential to differentiate CG cancer from BPH.
References


