Role of DWI in cervical cancer for prediction and monitoring of chemoradiotherapy response

Poster No.: B-0665
Congress: ECR 2015
Type: Scientific Paper
Authors: P. Kala, D. V. Bhargavi, R. Avantsa, G. Narayan; Bangalore/IN
Keywords: Genital / Reproductive system female, Pelvis, Oncology, MR, MR-Diffusion/Perfusion, Diagnostic procedure, Chemotherapy, Brachytherapy, Cancer, Multidisciplinary cancer care, Neoplasia
DOI: 10.1594/ecr2015/B-0665

Any information contained in this pdf file is automatically generated from digital material submitted to EPOS by third parties in the form of scientific presentations. References to any names, marks, products, or services of third parties or hypertext links to third-party sites or information are provided solely as a convenience to you and do not in any way constitute or imply ECR's endorsement, sponsorship or recommendation of the third party, information, product or service. ECR is not responsible for the content of these pages and does not make any representations regarding the content or accuracy of material in this file.

As per copyright regulations, any unauthorised use of the material or parts thereof as well as commercial reproduction or multiple distribution by any traditional or electronically based reproduction/publication method is strictly prohibited.

You agree to defend, indemnify, and hold ECR harmless from and against any and all claims, damages, costs, and expenses, including attorneys' fees, arising from or related to your use of these pages.

Please note: Links to movies, ppt slideshows and any other multimedia files are not available in the pdf version of presentations.

www.myESR.org
Purpose

DW-MRI has the potential to provide a standardized imaging measurement in therapeutic response evaluation. We investigate the possibility of DWI as an imaging bio marker and evaluate its ability to measure tumor response in carcinoma cervix.

Aims:

- To measure the apparent diffusion coefficient (ADC) values in cervical cancers
- To measure serial apparent diffusion coefficient (ADC) values for cervical cancer before, during and after chemo radiotherapy.
- To correlate the ADC values with loco regional outcome.
- To investigate the role of diffusion-weighted imaging (DWI) in predicting and monitoring chemo radiotherapy response in cervical carcinoma.

Methods and materials

Study was approved by an independent ethical committee. 30 patients with carcinoma cervix, who underwent chemo radiation therapy were examined with pelvic MRI and DWI before initiation of chemo radiation, after completing external beam radiotherapy and following completion of brachytherapy with a 1.5-T MR scanner and a 16 channel torso coil.

MR Imaging protocol consisted of pulse sequences, with and without contrast, with parameters as shown in Table 1 & 2.

Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>T2</th>
<th>T2 CERVIX (axis of cervix)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AXIAL</td>
<td>AXIAL</td>
</tr>
<tr>
<td>TR/TE (ms)</td>
<td>10/4.6</td>
<td>420/80</td>
</tr>
<tr>
<td>Slice thickness (mm)</td>
<td>7</td>
<td>7</td>
</tr>
</tbody>
</table>
Field of view (AP-mm) | 256 | 305 | 119 | 200 | 305 | 260 | 79 | 200

Interslice gap (mm) | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1

Matrix | 208X127 | 252X202 | 300X312 | 268X175 | 252X202 | 368X295 | 256X189 | 268X172

Table 2

<table>
<thead>
<tr>
<th>Parameters</th>
<th>T1 POST GAD</th>
<th>DWI(b0&amp;b1000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAGITTAL</td>
<td>597/10</td>
<td>691/10</td>
</tr>
<tr>
<td>CORONAL</td>
<td>691/10</td>
<td>1296/59</td>
</tr>
<tr>
<td>AXIAL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TR/TE(ms)</td>
<td>3.2</td>
<td>3.2</td>
</tr>
<tr>
<td>Slice thickness(mm)</td>
<td>3.2</td>
<td>3.2</td>
</tr>
<tr>
<td>Field of view (AP-mm)</td>
<td>200</td>
<td>200</td>
</tr>
<tr>
<td>Interslice gap (mm)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Matrix</td>
<td>276X165</td>
<td>320X152</td>
</tr>
<tr>
<td></td>
<td></td>
<td>124X100</td>
</tr>
</tbody>
</table>

**Image analysis:**

Treatment response was determined by comparing pre and post treatment conventional MR images. The ADC values from diffusion sequences before, during and after chemo radiotherapy were measured and compared. The apparent diffusion coefficient (ADC) values in the tumour, normal gluteus muscle and normal rectal mucosa were automatically calculated by manual placement of the region of interest (ROI). The tumour size and tumour volume were measured at each therapeutic time based on T2W images.

Final or mid treatment tumour size or volume response (%) were calculated using the equation: \( \frac{\text{pre-diameter(volume) - post-diameter(volume)}}{\text{pre-diameter(volume)}} \times 100 \) or \( \frac{\text{pre-diameter(volume) - mid-diameter(volume)}}{\text{pre-diameter(volume)}} \times 100 \).

Final or mid treatment change in tumour ADC values (%) were calculated using the equation: \( \frac{\text{post ADC - pre ADC}}{\text{pre ADC}} \times 100 \) or \( \frac{\text{mid ADC - pre ADC}}{\text{pre ADC}} \times 100 \).
Analysis of variance (ANOVA) and Student t test has been used to compare the ADC, size and volume parameters between the different response groups. The response to treatment was determined by comparing pretreatment and post treatment conventional MR images. Based on the response to treatment patients were categorized into complete, good and partial response groups. Patients with no residual tumour were considered as complete response group. Patients with more than 60% of final tumour size response were concluded as good response group and those with less than 60% as partial response group.

**Results**

Most of the patients were among 41-60 years (63.3 %), with mean age of 51.63±9.63 years.

**Distribution of patients according to treatment type**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No. of patients(n=30)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCRT</td>
<td>22</td>
<td>73.3</td>
</tr>
<tr>
<td>Neoadjuvant chemotherapy +CCR</td>
<td>8</td>
<td>26.7</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>30</strong></td>
<td><strong>100.0</strong></td>
</tr>
</tbody>
</table>

**Distribution of patients according to treatment response**

<table>
<thead>
<tr>
<th>Response group</th>
<th>No. of patients(n=30)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete Response</td>
<td>2</td>
<td>6.7</td>
</tr>
<tr>
<td>Good Response</td>
<td>17</td>
<td>56.7</td>
</tr>
<tr>
<td>Partial Response</td>
<td>11</td>
<td>36.7</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>30</strong></td>
<td><strong>100.0</strong></td>
</tr>
</tbody>
</table>

Pre, mid and post treatment comparative response evaluation of tumour size, volume and ADC. Table 1.
A significant difference was found between pre-Tx and mid-Tx and between pre-Tx and post-Tx, mean tumour diameter, volumes and tumour ADC's.

**Correlation of %Tumor ADC change with % tumor size and volume responses:** Table 2,3&4

**Comparison of tumor diameter and % size response between the response groups:**

The post treatment mean tumor diameter of the complete response (CR) and good response (GR) groups were significantly lower than that of partial response (PR) group (p<0.001).

The % final size response of the complete response (CR) and good response (GR) groups were significantly greater than that of partial response (PR) group (p<0.001).

**Comparison of tumor volume and % volume response between the response groups:**

The pretreatment mean tumor volume of the complete response (CR) and good response(GR) groups were larger than that of partial response (PR) group, but there was no significant difference between them(p=0.418).

The mid treatment and post treatment mean tumor volume of the complete response (CR) and good response (GR) groups were lower than that of partial response (PR) group with suggestive significance statistically (p=0.094 ;p=0.004).

**Comparison of tumor ADC and % ADC change between the response groups:**

The pretreatment; mid treatment and post treatment mean tumor ADC of the complete response (CR) and good response (GR) groups were statistically significant than that of partial response (PR) group (p=0.030; p=0.042; and p=0.004 respectively).

**Comparison of tumor, gluteus muscle and rectal mucosa ADC at each therapeutic time:**

There was statistically significant difference between the mean ADC values of tumor to gluteus muscle and rectal mucosa at pre-Tx and mid-Tx ( both P= 0.0001 and P= 0.0004 respectively) but there was no significant difference between the ADC values at post - Tx (P = 0.76 & P = 1.5 respectively).
Discussion:

Several studies have found that the mean ADC value of cervical tumor is significantly lower than that of normal cervical tissue.

Harry et al. in a recent study has evaluated DW-MRI as an early response indicator in women receiving chemoradiation for advanced cervical cancer. In their study, DW-MRI was carried out in 20 women with advanced cervical cancer prior to chemoradiation, and repeated 2 weeks into therapy and again at the conclusion of therapy. The mean ADC values for each measurement were correlated with final tumour response as determined by volumetric assessment of tumour size using MR imaging and conventional clinical response(48). It was found that the ADC values after 2 weeks of therapy correlated with eventual MR response ($p = 0.048$) and clinical response ($p = 0.009$), as did the change in ADC values after 2 weeks of therapy ($p = 0.01$ for MR response; $p = 0.03$ for clinical response).

Hyun et al found that tumor ADCs at mid-Tx had a significant correlation with the final size response but pre-Tx ADC values were not associated with final size response(3). Both pre and mid-Tx ADCs did not show significant correlation with the final tumour volume response. The changes in tumor ADCs at mid -Tx had a significant correlation with the final size response, however mid -Tx ADC changes were not associated with the final volume response. Hyun et al demonstrated no statistical difference in mean tumor ADCs at pre-Tx between responder and non-responder groups.

Correlations obtained in our study were consistent with that of Harry and Hyun with a significant and moderate positive linear correlation between the tumor ADCs at pre-Tx, mid-Tx and post -Tx and the final size response( Pearson coefficient = 0.391, 0.402 , 0.389 respectively and P value= 0.033, 0.028, 0.034 respectively).

Images for this section:
**Fig. 1:** Conventional MR images (a-f) of a patient with uterine cervical carcinoma showing partial response to chemo radiation therapy. The sagittal and axial T2W images at pre-Tx (a, b), mid-Tx(c, d) and post-Tx (e, f) illustrates consecutive reduction in the tumor size.
**Fig. 2:** Diffusion weighted images (g-l) of the patient in Fig.1 with uterine cervical carcinoma showing partial response to chemo radiation therapy. On corresponding ADC maps, the tumor illustrates serial increase in the ADC values with 1.1 at pre-Tx (g, h), 1.3 at mid-Tx (i, j) and 1.5 x 10-3 mm2/s at post-Tx (k, l).
Fig. 3: Conventional MR images (a-f) of a woman with uterine cervical carcinoma showing good response to chemo radiation therapy. The sagittal and axial T2W images at pre-Tx (a, b), mid-Tx (c, d) and post-Tx (e, f) illustrates consecutive reduction in the tumor size.
**Fig. 4:** Diffusion weighted images (g-l) of the same woman in Fig.3 with uterine cervical carcinoma showing good response to chemo radiation therapy. On corresponding ADC maps, the tumor illustrates serial increase in the ADC values with 0.7 at pre-Tx (g, h), 1.4 at mid-Tx (i, j) and $1.5 \times 10^{-3}$ mm$^2$/s at post-Tx(k, l).
Fig. 5: Conventional MR images (a-f) of uterine cervical carcinoma patient showing complete response to chemo radiation therapy. The sagittal and axial T2W images at pre-Tx (a, b), mid-Tx(c, d) and post-Tx (e, f) illustrates near complete reduction in the tumor size.
Fig. 6: Diffusion weighted images (g-l) of uterine cervical carcinoma patient showing complete response to chemo radiation therapy. On corresponding ADC maps, the tumor illustrates significant serial increase in the ADC values with 0.8 at pre-Tx (g, h), 1.5 at mid-Tx (i, j) and $1.6 \times 10^{-3}$ mm$^2$/s at post-Tx(k, l).
Table 1: Pre, mid and post treatment comparative response evaluation of tumour size, volume and ADC.

<table>
<thead>
<tr>
<th>Pair</th>
<th>Pearson correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
</tr>
<tr>
<td></td>
<td>r value</td>
</tr>
</tbody>
</table>

Table 2: Correlation of Tumor ADC with % final size response and %final volume response

<table>
<thead>
<tr>
<th>Pair</th>
<th>Pearson correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r value</td>
</tr>
</tbody>
</table>

Table 3: Correlation of %Tumor ADC change with % tumor size response
Table 4: Correlation of %Tumor ADC change with % tumor volume response

<table>
<thead>
<tr>
<th>Pair</th>
<th>Pearson correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r value</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The addition of diffusion weighted imaging to the conventional magnetic resonance imaging protocol allows precise assessment of uterine cervical carcinoma, from lesion detection and characterization to staging of tumor. When used in conjunction with apparent diffusion coefficient mapping, diffusion weighted imaging is a powerful tool with the potential for early and accurate prediction, assessment and monitoring of response to chemo radiation therapy.

Based on our data we found that:

# Most of the patients with uterine cervical carcinoma are in the age group of 51-60 years and belong to FIGO stage II B.

# The uterine cervical tumor demonstrates restriction on DW images and significantly lower values on ADC maps.

# There was a serial increase in the tumor ADC values along with corresponding decrease in the tumor diameters and volumes during the chemo radiation therapy.

# A significant and moderate positive linear correlation was found between the tumor ADCs and the final size response and volume response at pre-Tx, mid-Tx and post-Tx.

# The pre, mid and post treatment mean tumor ADCs showed significant differences between response groups being larger in the complete response (CR) and good response (GR) groups than that of partial response (PR) group. This suggests that tumors with high diffusion values will respond better to therapy than low diffusion values.

# A significant and moderate positive correlation was found between mid-Tx tumor ADC changes and the final tumor size and volume responses, indicating that patients with greater mid-Tx tumor ADC changes respond better to therapy than patients with lesser ADC changes.

# The mid and post treatment tumor diameters and volumes compared to the pretreatment tumor diameter and volume showed significant difference between the response groups being lower in complete and good response groups than that of partial response (PR) group. Hence the patients with lower mid treatment tumor diameter and volumes show better response to therapy.

# The mid and final size and volume % responses showed significant differences between response groups being greater in the complete response (CR) and good response (GR)
groups than that of partial response (PR) group. This indicates that **patients with greater mid size and volume responses respond better to therapy.**

# There was no significant difference in tumor ADC values when evaluated for other parameters like parametrial and vaginal invasion, lymph nodal involvement and FIGO stage. Hence **ADC mapping is less useful in predicting the extension and staging of uterine cervical carcinoma.**

# There was no significant difference in tumor ADC values and % tumor ADC changes with the addition of neoadjuvant chemotherapy to the routine chemo radiotherapy protocol concluding that the **neoadjuvant chemotherapy does not alter the treatment outcome in uterine cervical carcinoma.**

**Personal information**

Dr Prachi Kala, MD.
Sectional Imaging division, Department of Radiology,
Vydehi institute of medical sciences, Bangalore, India.
prachi_kala@yahoo.com

Dr Vidya Bhargavi,
Resident, Department of radiology,
Vydehi institute of medical sciences, Bangalore, India.

Dr Rohini Avantsa, MD.
Department of radiology,
Vydehi institute of medical sciences, Bangalore, India.
rkgayatri5@gmail.com
References


