Detection of early local recurrence of head and neck squamous cell carcinoma with diffusion weighted MRI and FDG PET/CT after radiotherapy: correlation between ADC and SUV values.

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Aims and objectives

Differentiation of post-treatment changes from recurrence of head and neck squamous cell carcinoma (HNSCC) on computed tomography (CT) or magnetic resonance (MR) images is generally not possible. Recurrent tumors and post-treatment changes may show similar appearances on routine MR imaging.

Diffusion weighted magnetic resonance imaging (DW-MRI) and ADC value have better results than routine MR imaging to differentiate recurrences from post-treatment changes. Fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) is a functional imaging method, and measures increased cellular glucose metabolism as expressed by the standardized uptake value (SUV) [1]. At a tissue level FDG uptake is correlated with the number of viable tumor cells and their metabolic activity [2].

The correlation between DW-MRI and PET/CT has been recently researched in evaluation of head and neck cancer [1-3]. Nevertheless, to our knowledge, there have been no reports about diagnostic significance comparing early recurrence and post-radiation changes in FDG uptake and ADC obtained in the same patient with HNSCC. Therefore, in this paper we compared them to define their diagnostic significance for detection of recurrence.
Methods and materials

From a computerized search of the PACS archives and medical records of our institution between November 2011 and January 2014, we identified 32 adult patients with histologically proven HNSCC who were treated with radiotherapy and had both DWI-MRI and FDG PET/CT. Three patients were excluded because of poor DW-MRI quality. Six patients were excluded because they did not have biopsy-proven diagnosis. Due to possible sampling errors of biopsy, the post treatment changes were also followed for at least 6 months. Finally 23 patients who had biopsy-proven diagnosis after radiotherapy, 3 women and 20 men, with a median age of 65 years (range 19-81 years) were included in the study. All patients were treated with radiotherapy: alone (n=9), after surgery (n=6), or with chemotherapy at the same time (n=8). Median delay times between radiotherapy and MR imaging, FDG PET/CT were 71 days (range 43-98 days) and 75 days (range 44-103 days) respectively. Median delay time between two examinations was 6 days (range 1-12 days). The median follow-up of the patients was 14.5 months (range 7-26.7 months).

All measurements were made blind to clinical data, and histopathology. MR images were analyzed by one reader who was a radiologist with 6 years experience in head and neck MR imaging. One reader who was a nuclear medicine specialist with 5 years experience in PET/CT analyzed PET/CT images. All images were evaluated in the transverse plane to allow comparison between MR and PET/CT images. The images were reviewed with/ by consensus between 2 readers.

We measured 3 ROI with similar size from the solid portion of the mass to obtain mean ADC_{mean} value in correspondence with contrast enhanced T1-weighted images. To avoid necrosis or cystic parts of the tumors, measurements of ADC were illustrated on the corresponding T2-weighted images. SUV_{max} was the maximum tissue concentration of FDG in the ROI. A ROI was placed with the aid of contrast enhanced T1-weighted and T2-weighted images that were used to identify the same anatomical level of the DW-MRI (Figure 1).
**Fig. 1:** Transverse FDG PET/CT and MR images of 70-year old patient with laryngeal tumor after radiotherapy. PET (A), fused PET/CT (B), and low dose CT demonstrate positive focus (SUVmax value is 15.9). T2WI (D), postcontrast T1WI (E) show heterogeneous enhanced lesion. ADC map (F) shows low signal intensity at the site of lesion with a mean ADCmean value of 0.72 x10-3 mm2/s. Biopsy revealed recurrence of tumor.
Results

According to the pathologic diagnosis and clinical and radiological follow-up recurrence was detected in the 12 patients, and post-treatment changes were found in 11 patients. Otherwise, no significant difference was observed in the mean age, the mean ROI size, and the mean interval from completion of radiotherapy to post-treatment imaging between the recurrence group and the group with post-treatment changes.

Table 1 summarizes the median and diagnostic values of ADC$_{\text{mean}}$ and SUV$_{\text{max}}$ in this study population. The median ADC$_{\text{mean}}$ values in the patients with recurrence were significantly lower than in the patients with post-treatment changes (0.73 vs. $1.35 \times 10^{-3}$ mm$^2$/s, respectively; p<0.001) (Figure 3A).

The mean SUV$_{\text{max}}$ values in the patents with recurrence were significantly higher than in the patients with post-treatment changes (15.45 vs. 4.70, respectively; p<0.001).

Cut-off value for ADC$_{\text{mean}}$ was $0.95 \times 10^{-3}$ mm$^2$/s to discriminate recurrence and post-treatment changes and statistically significant (p<0.001) with an AUC =0.924 (0.734-0.990). The sensitivity, specificity, and accuracy of the cut-off value were 100% (73.4-100.0), 72.73% (39.1-93.7), and 86.96% respectively.

Cut-off value for SUV$_{\text{max}}$ was 7.6 to discriminate recurrence and post-treatment changes and statistically significant (p<0.001) with an AUC=0.981 (0.818-0.984). The sensitivity, specificity, and accuracy of the cut-off value were 91.67% (61.5-98.6), 100.0% (71.3-100.0), and 91.30% respectively (Figure 3B).

There was no statistical difference between AUC values of SUV and ADC (p=0.342). However a moderate negative correlation between the ADC$_{\text{mean}}$ and the SUV$_{\text{max}}$ values of the patients in the post-treatment changes group was found (r= -0.691; p=0.019). Nevertheless there was no significant correlation between the ADC$_{\text{mean}}$ and the SUV$_{\text{max}}$ values of the patients in the recurrence group (r=0.341; p=0.278).
Fig. 2: Box-and-whisker plots of the ADCmean (A) and SUVmax (B) values for post-treatment changes and recurrence groups.

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Table 1: ADC\textsubscript{mean} and SUV\textsubscript{max} Values of Recurrence and Post-treatment Changes

<table>
<thead>
<tr>
<th></th>
<th>Recurrence (n=12)</th>
<th>Post-treatment Changes (n=11)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ADC\textsubscript{mean}</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Median</td>
<td>0.73</td>
<td>1.35</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Min</td>
<td>0.67</td>
<td>0.84</td>
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</tr>
<tr>
<td>Max</td>
<td>0.95</td>
<td>3.37</td>
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<tr>
<td><strong>SUV\textsubscript{max}</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>15.45</td>
<td>4.70</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Min</td>
<td>6.2</td>
<td>1.8</td>
<td></td>
</tr>
<tr>
<td>Max</td>
<td>26.5</td>
<td>7.6</td>
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Cut-off values

<table>
<thead>
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<th>ADC\textsubscript{mean}</th>
<th>Recurrence</th>
<th>Post-treatment Changes</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤0.95</td>
<td>12 (80%)</td>
<td>3 (20%)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>&gt;0.95</td>
<td>0 (0%)</td>
<td>8 (100%)</td>
<td></td>
</tr>
<tr>
<td>SUV\textsubscript{max}</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;7.6</td>
<td>1 (9.1%)</td>
<td>10 (90.9%)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>≥7.6</td>
<td>11 (91.7%)</td>
<td>1 (8.3%)</td>
<td></td>
</tr>
</tbody>
</table>

ADC\textsubscript{mean} indicates apparent diffusion coefficient ($\times 10^{-3}$ mm$^2$/s)
SUV\textsubscript{max}, maximum standardized uptake value
* Statistically significant
Conclusion

A few studies have already shown the advantages of DW-MRI and PET/CT in distinguishing recurrent tumor from post-treatment changes in head and neck cancer [1, 4-6]. Our data was collected in a more homogeneous and narrow time interval between imaging and treatment (range 43-103 days).

This study shows that both methods have highly accurate ability to diagnose recurrence and there is no statistically significant difference between diagnostic values of these methods (p=0.342), therefore any of these methods can be used during follow-up. There is a moderate negative correlation in the post-treatment changes group (r= -0.691; p=0.019). The negative correlation in the post-treatment group may be related with the small number of viable cells and increased extracellular water component. In the recurrent group, micro-structural environment that includes microscopic necrosis areas still affects ADC\textsubscript{mean} value to a different degree. SUV\textsubscript{max} values depend on the number of viable tumor cells and their metabolic activity, and are not affected by the micro-structural environment as ADC\textsubscript{mean} values are.

Our study revealed that PET/CT and DW-MRI are effective methods to distinguish recurrence of HNSCC from post-treatment changes, and they have similar and highly accurate results. Functional imaging techniques should be added to daily clinical routine to increase diagnostic accuracy of routine imaging. SUV\textsubscript{max} and ADC\textsubscript{mean} values are independent parameters in recurrent HNSCC.
References

Reference:


