Hybrid F-MISO PET/MRI for radiation therapy response assessment in cervix cancer

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Starting Point & Purpose

Purpose:

• investigate spatio-temporal stability of cervix cancer characteristics by repetitive multimodal/multiparametric PET and MR imaging
  – Tracer: F$^{18}$-MISO (hypoxia)

• Previous study: PET/CT + MR
  – poor patient compliance

• Current study: Hybrid PET/MR
  – Biograph mMR Scanner (SIEMENS)

• Study concept was conserved

[P. Georg, P. Andrzejewski et al., 2017, MIBI in press]
Study Concept

baseline | time point 1 | time point 2 | follow up
FMISO PET/MR | FMISO PET/MR | FMISO PET/MR | FMISO PET/MR

week 0 | week 1-5 | week 6&7 | week 19
external beam radiotherapy | brachytherapy | concomitant chemotherapy

4 imaging time points (BL / TP1 / TP2 / FU)

Obtained modalities:

T2w/PET   DCE   ADC   K\text{trans}   ABrix   iAUC
Materials & Methods

• 8 patients entered

Statistical Evaluation:
  – change of GTV
  – mean values
  – histogram-based parameters
  – voxel-by-voxel analysis
    → Intra-TP
    → Inter-TP
  – subvolume analysis:
    → Sørensen–Dice coefficients of thresholded regions
Change of GTV

- FIGO stage: IIB - IVA

![Graph showing change of GTV over time with PET/MR and PET/CT+MR comparisons.]

![Images of transversal and sagittal views of medical scans.]

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Change of Multimodal Parameters

- change of the mean value over the whole GTV

<table>
<thead>
<tr>
<th>mean</th>
<th>ADC</th>
<th>iAUC</th>
<th>$k^{\text{trans}}$</th>
<th>$A_{\text{Brix}}$</th>
<th>DCE$_{1\text{min}}$</th>
<th>T2w</th>
<th>PET TBR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>mean</td>
</tr>
<tr>
<td>BL-TP1</td>
<td>16%</td>
<td>n. sign.</td>
<td>n. sign.</td>
<td>n. sign.</td>
<td>15%</td>
<td>n. sign.</td>
<td>mean</td>
</tr>
<tr>
<td>BL-TP2</td>
<td>24%</td>
<td>n. sign.</td>
<td>n. sign.</td>
<td>n. sign.</td>
<td>n. sign.</td>
<td>-21%</td>
<td>-27%</td>
</tr>
<tr>
<td>BL-FU</td>
<td>28%</td>
<td>-24%</td>
<td>-37%</td>
<td>n. sign.</td>
<td>n. sign.</td>
<td>-19%</td>
<td>n. sign.</td>
</tr>
<tr>
<td>TP1-TP2</td>
<td>n. sign.</td>
<td>n. sign.</td>
<td>-28%</td>
<td>n. sign.</td>
<td>n. sign.</td>
<td>-32%</td>
<td>-26%</td>
</tr>
<tr>
<td>TP1-FU</td>
<td>n. sign.</td>
<td>n. sign.</td>
<td>n. sign.</td>
<td>n. sign.</td>
<td>n. sign.</td>
<td>-15%</td>
<td>n. sign.</td>
</tr>
<tr>
<td>TP2-FU</td>
<td>n. sign.</td>
<td>n. sign.</td>
<td>n. sign.</td>
<td>n. sign.</td>
<td>n. sign.</td>
<td>-15%</td>
<td>-25%</td>
</tr>
</tbody>
</table>
Histogram Parameters of ADC

Kurtosis

Skewness

BL  TP1  TP2  FU

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Histogram Parameters

- **Skewness**

- **Kurtosis**
  
  $A_{Brix}$: sign. drop TP1-TP2: $-25\%$
  
  $DCE_{1\text{min}}$: sign. drop: $+1,26(\text{BL}) \mid +0,72(\text{TP1}) \mid -0,66(\text{TP2})$
Voxel by Voxel Analysis: INTER-TIMEPOINT

all modalities showed small positive self-correlation coefficients of 0.2 to 0.3

<table>
<thead>
<tr>
<th>PET–PET correlation</th>
<th>all GTV voxels</th>
<th>thresholded (&gt;1.4 TBR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BL-TP1</td>
<td>+0.6 ± 0.1</td>
<td>+ 0.5 ± 0.2</td>
</tr>
<tr>
<td>TP1-TP2</td>
<td>+0.6 ± 0.3</td>
<td>+ 0.5 ± 0.2</td>
</tr>
<tr>
<td>TP2-FU</td>
<td>+0.4 ± 0.4</td>
<td>+ 0.4 ± 0.4</td>
</tr>
<tr>
<td>Over all</td>
<td>+0.5 ± 0.2</td>
<td>+ 0.5 ± 0.3</td>
</tr>
</tbody>
</table>

PET tumor to background ratio

![Graph showing PET tumor to background ratio with different markers for BL&TP1, TP1&TP2, and TP2&FU]
Voxel by Voxel Analysis: INTRA-TIMEPOINT

$DCE_{1\text{min}}, K^{\text{trans}}, iAUC$ and $A_{\text{Brix}}$ showed positive correlation coefficients around 0.5 to 0.6

$A_{\text{Brix}}$–FMISO correlation:

• FMISO & hypoxia

• $A_{\text{Brix}}$ & hypoxia [Fjeldbo et al., 2016]
No correlation of DCE-derived parameters ($A_{Brix}/K_{trans}/iAUC$) with FMISO could be observed

Fjeldbo et al., 2016
DICE Coefficients of Subvolumes

**DICE coefficient - PET**

- BL-TP1
- TP1-TP2
- TP2-FU

- **PET/CT+MR study**
- **TH 1.4**
- **TH 2.0**

**Graphs:**
- Transversal
- Coronal
- Saggital
Conclusion

• Hybrid PET/MR facilitates multimodality imaging research
  – Logistic challenges with PET/CT and MR
• $A_{\text{Brix}}$ provides complementary information to FMISO-uptake
• Shortcoming: so far few patients
  – Larger patient numbers in multicentric studies?
• At time of brachytherapy boost hypoxic subvolumes largely reduced

Thank you for your attention
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and many others ......
References

• Georg, P., Andrzejewski, P. *et al.* Changes in tumor biology during chemoradiation of cervix cancer assessed by multiparametric MRI and hypoxia PET. *MIBI (in press)*