“Mutation stratification of desmoid-type fibromatosis using a radiomics approach – preliminary results”

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Disclosure

Non-profit organisation

STICHTING S COOLSINGEL
The vast majority of desmoid tumors harbor a *CTNNB1* mutation

- About 80-90% of DTF tumors harbor a mutation in the *CTNNB1* (β-catenin) gene\(^1\)
- Supportive diagnostic tool
- Prognostic value?
  - S45F *CTNNB1* mutations have higher recurrence rates\(^2-5\)
The traditional diagnostic pathway of DTF

1. Symptoms
2. Doctors visit
3. Imaging
   - IHC β-catenin stain
   - Biopsy-histological diagnosis
4. CTNNB1 mutation
   - Next generation sequencing
5. Sanger sequencing
6. Definite diagnosis
7. Treatment
Radiomics – make use of conventional imaging methods

- Identification of imaging features that serve as molecular surrogates
- Non-invasive method
- Widely available (pre-treatment) images
- 3D (multiple planes)
Radiomics – previous studies

Non-small cell lung cancer

Gevaert et al. 2017

- Prediction of epidermal growth factor receptor (EGFR) mutation status
- n=186, CT imaging
- 16 semantic features significantly correlated with presence of EGFR (e.g. emphysema, distribution, nodules)
- AUC value 0.89

Clear-cell renal cell carcinoma

Karlo et al. 2014

- CT features and mutation status (VHL, PBRM1, SETD2, KDM5C, BAP1 genes)
- n=233, CT imaging
- VHL gene: well defined tumor margins (p=0.013), nodular tumor enhancement (p=0.021) and gross appearance of intratumoral vascularity (p=0.018)
- KDM5C and BAP1: renal vein invasion (p=0.022) and (p=0.046) respectively
Can we use radiomics in the clinical practice in the context of DTF?

Can we predict DTF $CTNNB1$ mutation status?
**Imaging – segmentation – feature extraction – prediction models**

<table>
<thead>
<tr>
<th>Online Multiparametric Database</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Lung PET" /></td>
</tr>
<tr>
<td><img src="image2.png" alt="Liver CT" /></td>
</tr>
<tr>
<td><img src="image3.png" alt="Head Desmoid T1-weighted MR" /></td>
</tr>
<tr>
<td><img src="image4.png" alt="Liver T2-weighted MR" /></td>
</tr>
<tr>
<td><img src="image5.png" alt="Brain T1-Weighted MR" /></td>
</tr>
<tr>
<td><img src="image6.png" alt="Mammogram" /></td>
</tr>
</tbody>
</table>
Imaging – segmentation – feature extraction – prediction models

Online Multiparametric Database

- Lung PET
- Liver CT
- Head Desmoid T1-weighted MR
- Liver T2-weighted MR
- Brain T1-Weighted MR
- Mammogram

Radiomics Platform

- Segmentation
- Classification
- Registration
- Feature Extraction

- Shape
- Intensity
- Advanced
Imaging – segmentation – feature extraction – prediction models
Using +/- 400 imaging features

**Semantic features**
e.g. age, gender, tumor location, pregnancy

**Computational features**
e.g. texture, shape, intensity and orientation
Can we predict DTF *CTNNB1* mutation status?

- Treatment naive extra-abdominal / abdominal wall DTF
- Known *CTNNB1* mutation or available formalin fixed parafin embedded samples
- T1 weighted MR imaging (spin-echo (SE) or gradient-echo (GRE))
- Between 2004 and 2017
Cross-validation model

Total: 49 Patients

Training: 80%

Test: 20%

Train Model

Repeat 100x

Evaluation
Can we predict DTF *CTNNB1* mutation status?

<table>
<thead>
<tr>
<th></th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>14</td>
</tr>
<tr>
<td>female</td>
<td>35</td>
</tr>
<tr>
<td><strong>Tumor location</strong></td>
<td></td>
</tr>
<tr>
<td>abdominal wall</td>
<td>12</td>
</tr>
<tr>
<td>extra-abdominal</td>
<td>37</td>
</tr>
<tr>
<td><strong>CTNNB1 mutation</strong></td>
<td></td>
</tr>
<tr>
<td>T41A</td>
<td>21</td>
</tr>
<tr>
<td>S45F</td>
<td>11</td>
</tr>
<tr>
<td>Wild-type</td>
<td>17</td>
</tr>
</tbody>
</table>
The radiomics technique has a promising role for differentiating WT tumors from tumors with a *CTNNB1* mutation.

<table>
<thead>
<tr>
<th></th>
<th>T41A</th>
<th>S45F</th>
<th>WT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity [95% CI]</td>
<td>0.26 [0.06 – 0.41]</td>
<td>0.11 [0.05 – 0.11]</td>
<td>0.42 [0.20 – 0.64]</td>
</tr>
<tr>
<td>Specificity [95% CI]</td>
<td>0.78 [0.61 – 0.94]</td>
<td>0.93 [0.83 – 1.02]</td>
<td>0.87 [0.75 – 0.99]</td>
</tr>
<tr>
<td>Area under the curve [95% CI]</td>
<td>0.58 [0.28 – 0.61]</td>
<td>0.58 [0.43 – 0.73]</td>
<td><strong>0.75 [0.61 – 0.88]</strong></td>
</tr>
</tbody>
</table>
Which features are relevant?

T-test

No single significant features after correction for multiple testing

Combination of features?
Conclusion from the pre-iminary results

- Promising role for differentiating WT tumors
Use of radiomics in clinical practice

- Prediction the *CTNNB1* mutation status does not change the diagnostic routine
- Biopsy is still needed to confirm the diagnosis

Can we differentiate DTF tumors from other soft tissue tumors?
Can we differentiate DTF tumors from other soft tissue tumors?

- Treatment naive fibromyxosarcoma, myxoid liposarcoma and leiomyosarcoma of the **extremities**
- T1 weighted MR imaging
- 2004 and 2017

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibromyxosarcoma</td>
<td>29</td>
</tr>
<tr>
<td>Myxoid liposarcoma</td>
<td>29</td>
</tr>
<tr>
<td>Leiomyosarcoma</td>
<td>29</td>
</tr>
</tbody>
</table>
Challenges using radiomics in the clinical practice of DTF

Discovery phase study, no validation of findings

**Imaging**
Differences in imaging protocols, different scanning methods
T1W MR images, extrapolate to other sequences

**DTF**
Small sample size, create a bigger cohort
Poor DNA quality not able to obtain *CTNNB1* mutations
Challenges using radiomics in the clinical practice of DTF

Radiomics

Learning curve in segmentation
Currently, semi-automatic segmentation → time consuming → automatic segmentation?
Inter- and intra observer differences
Inter and intra-observer variability
Inter and intra-observer variability

Original
Obs. 1, att. 1
Inter and intra-observer variability

Original  Obs. 1, att. 1  Obs. 1, att. 2
Inter and intra-observer variability
Radiomics is a promising new technique

Future perspectives
Large cohort (multiple institutes)
Inclusion of multiple sequences
Imaging of DTF using a standard imaging protocol

Optimizing the radiomics platform and analysis (include more imaging features)
Using radiomics to quantify tumor progression / regression (e.g. tumor enhancement) over time
References


https://github.com/MStarmans91/WORC

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