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Title: Mutation stratification of desmoid tumors using a radiogenomics approach

Authors

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Purpose Radiogenomics is a promising technique, correlating quantitative imaging features with molecular characteristics. This study evaluates the use of radiogenomics features extracted from T1 weighted Magnetic Resonance (T1w MR) images to predict CTNNB1 mutation status (T41A, S45F and wildtype) of desmoid-type fibromatosis (DTF) tumors.

Methods Approval from the Medical Ethics Committee of Erasmus MC in Rotterdam, the Netherlands was obtained for this study (MEC-2016-339). Cases of treatment naive extra-abdominal and abdominal wall DTF, with available digital T1w MR images, were selected from the pathology database of the Erasmus MC, Rotterdam, the Netherlands. Sanger sequencing on formalin fixed paraffin embedded material was performed to obtain CTNNB1 mutation status in case of undetermined mutation status. Tumors were semi-automatically annotated on the anonymized T1w MR images by a single clinician. Features quantifying shape, intensity and texture, for a total of 424 per patient, were extracted from the images using the segmentations as region of interest. A Support Vector Machine (SVM) was trained and evaluated using these features in a 100x random split cross validation, with the training set consisting of 80% of the patients. For each mutation, an SVM was constructed using a one-vs.-all approach. Classification performance was assessed by the area under the receiver-operating-characteristic curve (AUC).

Results A total of 49 patients; 14 males and 35 females, with DTF located extra-abdominal (n=37) or in the abdominal wall (n=12) were included. Tumors harbored a T41A mutation in 21 cases, a S45F mutation in 11 cases and 17 tumors were considered to be wildtype tumors. The radiogenomics approach resulted in AUC 95% confidence intervals of [0.28, 0.61], [0.43, 0.73] and [0.61, 0.88] for classification of the T41A, S45F and wildtype mutations, respectively.

Conclusions The preliminary results of this radiogenomics model show the promising predictive value for classification of wildtype mutations, but could not differentiate between the various genetic mutations. The use of a larger, multi-center dataset with the use of additional MRI sequences and more advanced multi-class machine learning approaches could improve the radiogenomics model to develop a prediction model for DTF that can be used both in research and in clinical practice.