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EDITORIAL

Artificial intelligence and radiomics in desmoid-type fibromatosis: are we there yet?

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Desmoid-type fibromatosis (DF), a subgroup of rare mesenchymal tumors, constitutes around 0.03% of all diagnosed malignant tumors, most commonly affecting young women [1,2]. These DFs' are locally invasive with significant morbidity and a high risk for disease recurrence despite the lack of occurrence of distant metastasis [3]. On the molecular level, the vast majority of DFs harbor a *CTNNB1* somatic mutation with the most common reported mutations being T41A, S45F and S45P. These mutations have no known therapeutic impact yet but they serve as a prognostic tool with S45F mutations conferring the worst prognosis [4]. The clinical presentation of DF varies widely based on the tumor location in the abdomen or extremity with a palpable mass or pain, which then necessitates optimal diagnostic testing. Therefore, performing magnetic resonance imaging (MRI) is the preferred imaging modality for the diagnosis and characterization of DF patients. These usually feature the 'split fat sign', where the tumor is centered within the muscles and is surrounded by a rim of fat, with local muscle infiltration as well as the demonstration of the 'fascial tail sign', described by an extension through the fascial boundaries. On T1-weighted (T1w) and T2-weighted (T2w) sequences, DF tends to have an intermediate signal intensity while post-contrast injection MR images demonstrate a heterogeneous enhancement with the hypo-intense band-like morphology (reported in up to 90% of DFs) [5]. Nevertheless, conventional radiological techniques alone are currently unable to confirm the diagnosis of DF without the need to tissue biopsy for pathological and molecular confirmation. Recent guidelines on the management of DF patients opt for a 'wait and see' strategy in asymptomatic patients with the indication to initiate medical therapy in symptomatic or progressing tumors [6]. Once indicated, active medical therapy relies on conventional chemotherapy, targeted therapy (tyrosine kinase inhibitors) and novel agents such as gamma-secretase inhibitors with varying degrees of efficacy [4].

Recent advances in artificial intelligence (AI) and deep learning (DL) techniques have drastically revolutionized the medical and imaging field, most particularly in the optimization of the diagnostic and therapeutic process. One subset of the AI-based approaches in healthcare is radiomics, which is a growing field with the specific application of machine learning (ML) algorithms in the field of medical imaging [7]. Recent data have shown that the application of various radiomics models with a heavy amount of quantitative imaging is associated with a significant impact on both clinical and therapeutic outcomes but also could serve as an alternative tool for invasive or expensive procedures [8]. Various trials have assessed the role of radiomics in numerous types of malignant tumors such as breast cancer, colorectal cancer and Soft tissue sarcomas () [9–11]. In this paper, we shed light on the current published data on the application of AI including radiomics in DF patients.

First, radiomics can aid in the identification and diagnosis of DF without the need to apply invasive procedures. Timbergen et al. opted to assess the role of radiomics, through the creation of multiple prediction models by different ML approaches, in distinguishing DFs from other STS in 203 recruited patients [12]. One of the radiomics models, generated with the pre-treatment MRI T1-weighted (T1w) images, has successfully identified DF patients with a high accuracy in comparison to radiologists. Additional findings from this study are that the addition of other MRI sequences such as T2-w or T1w post-contrast injection did not enhance the models' performances. In another objective of this trial, the authors investigated the ability of this model to predict the *CTNNB1* mutation status of DF patients in an attempt to reduce the performance of time-consuming testing such as NGS (Next-generation sequencing) and to assess their prognosis. Nevertheless, the radiomics model failed

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to predict the *CTNNB1* mutation types (S45F, T41A and wild-type) of the DF [12]. This approach of radiogenomics has been also evaluated in 63 STS patients, where the natural evolution of STS evaluated on baseline MRIs was correlated with the different gene expression profiles using radiomics features [13]. Therefore, as one of the advantages of this AI-based tool, radiomics can serve, with the aid of MRI sequences, in the diagnosis of DF while there is still a lack in the possible identification of the *CTNNB1* mutation status.

Second, radiomics can predict disease progression in DF tumors undergoing systemic therapy, outperforming the standard RECIST criteria (Response Evaluation Criteria in Solid Tumors version 1.1) [14]. In DF patients treated with active anti-cancer drugs, an increased heterogeneity can occur on MRI images, reflecting increased necrosis before any volumetric alterations. This phenomenon is also observed in, progressing DF patients where an enhancement of the active component of the tumor is noted on imaging [2]. While the current validated response criteria have limited predictive capacity for early disease progression, radiomics enables early detection of heterogeneity of DF, through the quantification of architectural changes including shape and texture features [15]. For example, Liu et al. applied a web-based nomogram, incorporating three independent predictors of relapse of DFs (age, tumor diameter and number), in 385 patients to successfully predict recurrence-free survival [16]. In a multicentric study by the French sarcoma group, Crombe et al. further demonstrated retrospectively that a radiomics model, based on MRI data at baseline and after the first cycle of chemotherapy (T1w images)in 42 patients with progressing DFs, was significantly correlated with progression-free survival (PFS) (Hazard ratio (HR) $= 5.6$; $p = 0.003$). In contrast, the conventional response criteria (RECIST 1.1, CHOI, Cheson criteria) failed to show any significant correlation with PFS. The study that radiomics could predict volumetric progression months earlier than conventional criteria [14]. Then, another advantage of radiomics in DF is the ability to predict the risk of disease progression in the first 12 months, potentially improving survival outcomes.

With the recent advancements in the AI field, these two significant trials constitute a valuable opportunity for DF patients – rarely included in clinical trials - to indulge in the AI euphoria to improve their outcomes, despite the numerous challenges. While only MRI images were evaluated in DF patients, AI has demonstrated increasing effectiveness in the detection of numerous medical conditions such as pulmonary embolism or fractures, through CT scans and conventional radiographs. Given the ongoing approval of AI algorithms, multiple applications in DF management can be explored including the prediction of tumor response or survival outcomes based on the different treatment modalities, despite the rarity of DF. Furthermore, AI has the potential to detect the characteristics of low-risk DF with spontaneous regression, a condition occurring in 10–28% of DF patients, thereby preventing the use of unnecessary therapies [17]. Moreover, AI could also predict the *CTNNB1* mutation status and the risk of DF occurrence in high-risk patients with familial adenomatous polyposis, who carry the germline APC mutation. Future clinical trials incorporating novel AI algorithms could be tailored for desmoid-type fibromatosis (DF) with the goal of assisting radiologists in several key areas. These include improving the characterization of desmoid tumors among other abdominal tumors, enhancing the accuracy of tumor behavior prediction to minimize the use of unnecessary treatments and developing robust prognostic tools [18]. Collaborative, multicentric studies are essential to validate the robustness of radiomics across diverse patient populations and imaging platforms.

In conclusion, the implementation of DL models including radiomics under the wide umbrella of AI in healthcare can enhance the clinical and survival outcomes in cancer patients. In DF patients, these improved models can serve as tools to support the physicians in the early phase of the diagnostic process and predict the risk of relapse in patients undergoing active therapy. As we are only experiencing the "tip of the iceberg" in the AI revolution, these rare tumors must be prioritized to optimize their therapeutic plan and avoid unnecessary invasive procedures or toxic anti-cancer drugs. Ongoing trials should prospectively evaluate the clinical utility of radiomics, focusing not only on its ability to predict treatment response and disease progression but also on its potential to enhance personalized treatment strategies.

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