

ORIGINAL RESEARCH ARTICLE

Early results in the novel use of contrast-enhanced susceptibility-weighted imaging in the assessment of response and progression in desmoid fibromatosis: A pilot study in a specialized cancer institution

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Abstract

Routine radiologic reporting (RRR) often considers progressive desmoid tumors to have a higher proportion of T2-hyperintense and T1-shortened-enhancing components, while responsive or mature collagenized tumors demonstrate a higher proportion of T2-hypointense-non-enhancing components. We aim to determine the utility of the novel use of contrast-enhanced susceptibility-weighted imaging (CE-SWI) in Desmoid-Tumor treatment response assessment, distinguishing between the T1-shortening-enhancing/T2-hyperintense immature components from the T2-hypointense mature collagenized components. This pilot study included 10 single-lesion extremity desmoid fibromatosis patients undergoing standard-ofcare magnetic resonance imaging, including CE-SWI. Three-dimensional (3D) tumor segmentation was performed using MIM software in 48 volumes of interest. Maximum diameter, volume, and modified Choi (mChoi) measurements were computed from CE-SWI and T2-weighted image (T2-WI). Five first-order radiomic features, including mean, skewness, kurtosis, and 10th and 90th percentiles, were calculated using in-house developed software (CARPI-AF). (i) RECIST Progression: We observed two cases of progression according to the T2-WI-based Response Evaluation Criteria in Solid Tumors standard (RECIST). Interestingly, CE-SWI-based-volume and CE-SWIbased-mChoi predicted the same assessment 4.5 months earlier than T2-WI-based-RECIST. RRR assessed both cases as progression; (ii) RECIST Stability: Out of the eight patients classified as having stable disease by T2-WI-based-RECIST, four discrepant progressions were determined: three patients showed an increase greater than 25% of T2-WI-based-volume, and two patients showed an increase greater than 25% of CE-SWI-based-volume. Moreover, from the RECIST stable group, four discrepantpositive responses were predicted by CE-SWI-based-mChoi (three patients) and T2-WIbased-mChoi (four patients). RRR only assessed one patient as having progressive disease; (iii) First-Order Radiomics: CE-SWI detected 23% more 90th-percentile voxels than T2-WI, while T2-WI demonstrated 8.5% more 10th-percentile voxels than CE-SWI. Notably, expected first-order response/progression-related changes in 10th-percentile, 90th-percentile, mean, and skewness were present in 90% of cases. In conclusion, CE-SWI-based-volume and CE-SWI-based-mChoi measurements could

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Publisher's Note: AccScience Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations. improve the prediction of response/progression in desmoid tumors, enhancing the ability in discriminating between T2*hypointense-collagenized-mature and T1-shortened-enhancing immature components, respectively, in predominant mature responsive and immature progressive tumors, respectively. RRR is relatively insensitive to volumetric tumor changes before RECIST progression and tends to be better tuned with T2* signal and enhancement changes.

Keywords: Susceptibility weighted imaging; Desmoid fibromatosis; First order radiomics; Modified-Choi

1. Introduction

Desmoid tumors are rare mesenchymal neoplasms composed of a clonal proliferation of fibroblasts and myofibroblasts with intracellular collagen and poorly defined margins^[1-4]. These tumors are locally invasive soft-tissue lesions originating in connective tissue and express the intermediate filament vimentin but lack the expression of epithelial markers such as E-cadherin^[3].

Spontaneous regressions or prolonged stabilizations occur in about 66% of desmoid cases^[2]. Current guidelines recommend intervention on desmoid tumors only in cases of progression, morbidity, or symptoms. There is no consensus on the best therapeutic management of these tumors^[5]. Surgery should be avoided because of the difficulties of obtaining negative margins and the high risk of local recurrence^[2].

In concordance with published evidence^[2,6-8], subjective clinical imaging evaluations often consider progressive desmoid tumors to have a higher proportion of T2-hyperintense and T1-shortened-enhancing components, while responsive or mature collagenized tumors demonstrate a higher proportion of T2-hypointense-non-enhancing components. The increase of T2-hypointense elements is typically considered a sign of positive response irrespective of tumor size^[9-13] (Figure 1). In contrast, an increase in the T2-hyperintense and T1-shortened-enhancing components is often seen as a sign of progression that can precede enlargement^[10,12-14].

Contrast-enhanced susceptibility-weighted imaging (CE-SWI) is a 3D, high spatial resolution, velocitycorrected gradient echo magnetic resonance imaging (MRI) technique that uses magnitude and filtered-phase information, separately and in combination, to generate images^[15-18]. The susceptibility effect from molecules that have paramagnetic (deoxyhemoglobin, ferritin, and hemosiderin), diamagnetic (bone minerals, dystrophic calcifications, and oxyhemoglobin), or ferromagnetic (iron, nickel, and cobalt) properties are demonstrated as areas of signal loss^[15,17,18]. While the most common use of CE-SWI is for identifying small amounts of calcium and hemorrhage^[18,19], the soft tissue contrast offered by CE-SWI can allow for the characterization of fibrous and cellular components in desmoid fibromatosis.

This study aimed to determine the utility of the novel use of CE-SWI as a single sequence capable of simultaneously characterizing the Immature T2-hyperintense and T1-shortening enhancing and the mature T2-hypointense collagenized components, using volumetric measurements and first-order radiomic features compared against conventional T2-based Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1^[20-22] assessments for an improved response assessment in desmoid fibromatosis.

This study provides initial evidence outlining the novel use of CE-SWI as a single MRI sequence capable of providing insight regarding the underlying biological changes of responsive and progressive desmoid tumors using 3D volumetric assessment, allowing improved separation of T2-hypointense mature collagenized tumor from T2-hyperintense, T1-shortened-enhancing, immature, and progressive tumor components.

2. Methods

An Institutional Review Board (IRB)-approved waiver of consent was obtained for this retrospective study, including an initial pilot analysis of 10 single-lesion extremity desmoid fibromatosis patients undergoing standard-of-care MRI examinations in our institution. Diagnostic biopsy and pathologic confirmation of tumor histology were obtained in all cases at diagnosis. The MRI scans included advanced imaging sequences, including diffusion-weighted imaging/ apparent diffusion coefficient^[23,24], perfusion-weighted imaging with dynamic contrast enhancement (PWI/DCE)^[25,26], and CE-SWI, performed between March 2021 and May 2023.

CE-SWI and T2-STIR data were collected from each patient across multiple time points in their treatment. A 3D manual tumor segmentation was performed in 48 volumes of interest (VOIs) by an imaging-specialized research assistant (M.A.C.) and an experienced skeletal radiologist (R.V.) using MIM commercial software (version 7.1.4, MIM Software Inc., Cleveland, USA).

Data obtained from each VOI included maximum diameter, volume, and modified Choi (mChoi) measurements

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Figure 1. Comparison between contrast-enhanced susceptibility-weighted imaging (CE-SWI) (superior rows) and T2-STIR images (inferior rows) and their corresponding intensity histograms in a patient with desmoid fibromatosis undergoing treatment across 4-time points. The images from left to right demonstrate enhancement reduction and increased T2-hypointensity due to collagenization, as seen in responsive tumors. CE-SWI detected a more significant amount of voxels above the 90th percentile (right side of the histogram) relative to T2, while T2 demonstrated a higher detection of voxels below the 10th percentile (left side of the histogram) than CE-SWI.

from CE-SWI and T2-STIR sequences. mChoi values were estimated as a normalization quotient obtained by dividing an entire desmoid lesion's mean 3D intensity value by the adjacent standard muscle intensity value^[6,11,27]. An IBSI-compliant^[28,29] open-source in-house developed software (CARPI-AF: Cancer Radiomic and Perfusion Imaging Automated Framework) was used to automatically extract five firstorder radiomic features (mean, skewness, kurtosis, 10th and 90th percentiles) from the CE-SWI and T2 images. Before radiomic feature extraction, all images were preprocessed in CARPI-AF by performing interpolation to isotropic voxel spacing of 1 mm using B-spline and discretization using a fixed histogram bin count of 50^[30]. Finally, for each patient, the percentage of voxels accumulated below the 10th and above the 90th percentiles (10th and 90th percentile proportions) were computed for the 10th and 90th percentile cutoffs at the firsttime point in the patient's treatment.

Patient response was assessed using conventional RECIST as a reference standard and compared against T2-STIR and CE-SWI volumetric assessment, mChoi, first-order radiomic features, and routine radiologic reporting (RRR). Thresholds for progression and response were set at 20% and 30% for unidimensional RECIST and volumetric mChoi assessments^[11]. An increase of 25% and a decrease

of 50% were considered thresholds for progression and response, respectively, for 3D volumetric assessment^[11,31].

3. Results

This study included eight female and two male patients with an average age of 42 years (range 19 – 61 years). Five patients were treated with sorafenib, two with pazopanib, and three were undergoing active surveillance without therapy. Given the reduced pilot study sample size, we did not include an analysis of therapeutic efficacy but focused on the development of imaging biomarkers.

Of the 10 patients, two were considered true progression based on T2-based RECIST, while eight were deemed stable. No true T2-RECIST-based positive responses were included in this pilot study.

3.1. True T2-based RECIST progression

Two patients displayed true progression based on the T2-based RECIST reference standard (Figure 2, left panels). This same result was detected by CE-SWI volume and mChoi at an average of 4.5 months earlier than T2-based RECIST. According to RRR, CE-SWI volume, and mChoi, both cases were assessed as progressive. In



Figure 2. Left panels show true progression by T2-based Response Evaluation Criteria in Solid Tumors (RECIST), also detected by volume and mChoi with an average of 4.5 months earlier. Middle panels show stable RECIST with discrepancy assessment of progression by volume in two representative patients. Clinical radiologists (routine radiologic reporting [RRR]) are often insensitive to detect progression by volume change. Right panels show stable RECIST with discrepancy assessment of response by mChoi in two representative patients. Clinical radiologists (RRR) are very sensitive to changes in T2 signal and enhancement in correlation with the variation of mChoi values.

true progression cases, CE-SWI detected an average of 23% more voxels above the 90th percentile relative to T2, while T2 demonstrated an average of 8.5% more voxels below the 10th percentile than CE-SWI (Figure 3).

3.2. T2-based RECIST stability

3.2.1. RECIST stability with discrepant progression

Based on T2-based RECIST, four patients were determined as stable (Figure 2, middle panels). Progression was determined in these patients by an increase >25% of T2-based volume (in three patients) and CE-SWI-based volume (in two patients). Nevertheless, only one of the four progressive cases was able to be determined by RRR.

3.2.2. RECIST stability with a discrepant positive response

Four patients displayed stable T2-based RECIST with a discrepant positive response (Figure 2, right panels), as predicted by CE-SWI mChoi (in three patients) and T2 mChoi (in four patients). All cases assessed by mChoi as responding patients were also considered positive responses by RRR.

3.2.3. First-order radiomics

The expected trends associated with responding patients (Figure 4), including increasing 10th-percentile hypointense voxel proportion, decreasing 90th -percentile hyperintense

voxel proportion, decreasing mean, and increasing skewness, and the opposite trends in progressive disease patients, were present in at least one of these features in 9 out of 10 (90%) patients; all four expected trends were present in 3 out of 10 (30%) patients (Figure 5 and Table 1).

4. Discussion

This pilot study suggests that RRR-based desmoid tumor assessment is relatively insensitive to volumetric tumor changes preceding RECIST progression (Figure 2, middle panels). On the other hand, they tend to be better tuned with changes in T2-hypointensity as a measure of collagenization and with changes in T1-shorteningenhancement as a measure of progressive disease, which are manifested in parallel with the mChoi values, concerning both positive mChoi responses in stable RECIST and to mChoi progression in RECIST progression.

All eight cases of T2-RECIST stability (100%) had a discrepant evaluation of either progression by volume or positive response by mChoi (Figure 2), suggestive of the insensitivity of RECIST to detect the biologic changes displayed by desmoid tumors under systemic treatment or active surveillance.

First-order radiomic trends, including a higher percentage of hyperintense voxel proportion (above the 90th percentile) and earlier detection of progression by mChoi, suggest an



Figure 3. Left panels show a higher percentage of voxels above the 90th percentile in contrast-enhanced susceptibility-weighted imaging (CE-SWI) versus T2-STIR in an actively progressing lesion. Right panels show a higher percentage of voxels below the 10th percentile in T2 versus CE-SWI in a highly collagenized responsive tumor. On average, CE-SWI imaging captures 23% more 90th percentile voxels than T2.

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Figure 4. Plots of Response Evaluation Criteria in Solid Tumors, volume, modified Choi, and first-order radiomic features of a representative patient across treatment demonstrate expected response trends, including decreased mean, increased skewness, increased 10th percentile voxel proportion, and decreased 90th percentile voxel proportion.



Figure 5. First-order radiomic trends in six representative patients were observed for each of the three response categories (progression by Response Evaluation Criteria in Solid Tumors [RECIST] T2, stable RECIST discrepancy with progression, and stable RECIST discrepancy with response). The red boxes highlight the trends of first-order radiomic features concordant with the expected response trends.

Modality	Progression by RECIST T2				Stable RECIST discrepancy with progression								Stable RECIST discrepancy with response							
	Case 1		Case 2		Case 3		Case 4		Case 6		Case 10		Case 5		Case 7		Case 8		Case 9	
	SWI	T2	SWI	T2	SWI	T2	SWI	T2	SWI	T2	SWI	T2	SWI	T2	SWI	T2	SWI	T2	SWI	T2
Mean	Y	Y	Y	Ν	Ν	Ν	Ν	Y	Y	Y	Ν	Ν	Ν	Ν	Y	Y	Y	Y	Ν	N
Skewness	Ν	Ν	Y	Y	Ν	Ν	Y	Y	Ν	Ν	Ν	Y	Ν	Ν	Y	Y	Ν	Y	Ν	Y
10 th percentile	Y	Y	Y	Ν	Ν	Ν	Ν	Ν	Y	Y	Ν	Y	Ν	Y	Y	Y	Y	Y	Ν	Ν
90 th percentile	Y	Y	Y	Y	Ν	Ν	Ν	Y	Y	Y	Ν	Ν	Ν	Ν	Y	Y	Y	Y	Ν	Ν
Total	3	3	4	2	0	0	1	3	3	3	0	2	0	1	4	4	3	4	0	1

Table 1. Summary of trends in mean, skewness, 10th and 90th percentile proportions in CE-SWI and T2 and their concordance (Y/N) with response category for each of the 10 desmoid fibromatosis patients included in this study

Notes: Y: Yes; N: No; CE-SWI: Contrast-enhanced susceptibility-weighted imaging; RECIST: Response evaluation criteria in solid tumors.

overall performance advantage of CE-SWI volumetric and mChoi assessments over conventional T2-weighted equivalents and traditional RECIST. The observed results align with the statistical power expected from a small sample size, outlining the need for a larger population analysis to extend this pilot study.

5. Conclusion

RRR is relatively insensitive to volumetric tumor changes before RECIST progression and tends to be better tuned with T2* signal and enhancement changes. Our study suggests that the novel use of CE-SWI-based volumetric and mChoi measurements could improve the prediction of response/progression in desmoid tumors by providing a better assessment by means of 3D tumor size measurements and could enhance the discrimination between the mature collagenized component and the enhancing immature components, respectively, predominant in mature responsive and immature progressive disease. In line with these encouraging early results, a larger population study that includes multifocal disease as a disease of interest, enrols RECIST-based positive response cases, and performs treatment efficacy analysis is warranted.

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Conflict of interest

The authors declare that they have no competing interests.

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Ethics approval and consent to participate

An approved waiver of consent was obtained for this retrospective study.

Consent for publication

An IRB granted a waiver of informed consent for this study.

Availability of data

Data can be obtained from corresponding author following formal request.

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