

## MAJOR PAPER

# Development of a Surface Marker for Fractional Anisotropy Maps Using Wood in a Phantom Study

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**Purpose:** To improve imaging, a reliable setup method is critical for the accurate localization of lesions and surface markers. Because an anisotropic marker has not yet been validated for MRI, direct localization of surface markers is not yet feasible in fractional anisotropy (FA) maps. This study aimed to develop an anisotropic surface marker using wood for an FA map and to determine whether a wood marker is useful for various sequences.

**Methods:** Wood infiltrated with water was used to develop an anisotropic surface marker. The wood marker was compared with phantoms composed of clinically available markers, including MR-SPOTS Packets (Beekley Medical, Bristol, CT, USA), Breath Care Oral Refreshing Capsules (Kobayashi Pharmaceutical Co., Ltd., Osaka, Japan), and baby oil (Johnson & Johnson, New Brunswick, NJ, USA). Magnetic resonance images were acquired using the Achieva 3T TX MRI System (Philips HealthCare, Best, Netherlands) equipped with a QD head coil including  $T_1$ - and  $T_2$ -weighted imaging, proton-density-weighted imaging,  $T_2^*$ -weighted imaging,  $T_1$ -weighted imaging spectral pre-saturation with inversion recovery,  $T_2$ -weighted imaging spectral attenuated inversion recovery, proton-density-weighted imaging spectral attenuated inversion recovery, diffusion weighted imaging, and diffusion tensor imaging. Apparent diffusion coefficient, FA values, and signal-to-noise ratio (SNR) were measured and recorded, and the coefficient of variation was calculated for two consecutive imaging scans. The wood was observed using a microscope.

**Results:** Breath Care Oral Refreshing Capsules and baby oil were not observed in the FA map. The FA value of the MR-SPOTS Packets was 0.18. The FA value of the wood marker was 0.80. The coefficient of variation of the MR-SPOTS Packets and the wood marker were 0.0263 and 0.0013, respectively, in the FA map. Microscopic observation revealed a wood anisotropic structure.

**Conclusion:** The wood maker enabled direct localization in the FA map. Hence, wood markers may be useful to radiologists and contribute to obtaining useful findings.

**Keywords:** *diffusion tensor imaging, fractional anisotropy map, skin marker, surface marker*

## Introduction

Surface markers are used in MRI<sup>1</sup> to identify the location of masses<sup>2</sup> and sites of pain.<sup>3</sup> The markers can be attached to a reference point to designate the location of a target site in clinical findings, which are difficult to observe without a suitable marker for interpreting radiological images as they may not be

observed on imaging. Therefore, radiological technologists use markers over sites of symptoms or palpable masses before examinations. The markers are useful to radiologists in interpreting findings.

However, very few studies have examined conventional surface markers in various MRI sequences. Itoh et al.<sup>4</sup> investigated Breath Care Oral Refreshing Capsules (Breath Care; Kobayashi Pharmaceutical Co., Ltd., Osaka, Japan), which are inexpensive and readily available. Ebrahimi et al.<sup>5</sup> used MR-SPOTS Packets (MR-SPOTS; Beekley Medical, Bristol, CT, USA), which are commercially available markers. Takatsu et al.<sup>6</sup> suggested that even baby oil can be used to localize lesions in MRI.

Manganese chloride capsule markers have been used to localize lesions in  $T_1$ -weighted imaging ( $T_1$ WI) and in comparisons with diffusion tensor imaging (DTI).<sup>7</sup> The absence of useful markers for DTI required  $T_1$ WI acquisition and a

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comparison of images. Moreover, such comparisons would be impossible when imaging is not performed in the same direction.

The development of novel surface markers may lead to an improved interpretation of DTI findings. We performed a pilot study to verify the anisotropy of wood infiltrated with water through the tracheid. Our study aimed to develop a surface marker for DTI made from wood infiltrated with water, and to verify whether a wood marker is useful for various sequences in MRI. To date, a surface marker useful for DTI has not yet been made available. However, such a novel wood marker would be effective and enable direct localization for DTI purposes.

## Materials and Methods

### Phantom

MR-SPOTS, Breath Care, baby oil (Johnson & Johnson, New Brunswick, NJ, USA), and the wood marker (Chamaecyparis obtuse) were used as phantoms. MR-SPOTS, Breath Care, and baby oil have been previously used in research and the clinic. Chamaecyparis obtuse was provided by the Forestry and Forest Products Research Institute for use in this study.

Breath Care-, MR-SPOTS-, and baby oil-filled 5 mL syringes were used in the present study. A piece of dry wood,  $14 \times 14 \times 40 \text{ mm}^3$  in size, was boiled for 20 min and stored in a water-filled container for 7 days. The wood specimen was sealed in a polypropylene case using vinyl tape. The wood piece and other syringes were secured in the same polyvinyl alcohol-filled container (Fig. 1).

### Imaging

Images were acquired using an Achieva 3T TX MRI System (Philips HealthCare, Best, The Netherlands) equipped with a



**Fig. 1** Phantoms, left to right: 5 mL syringes filled with MR-SPOTS Packets (Beekley Medical, Bristol, CT, USA), Breath Care Oral Refreshing Capsule (Kobayashi Pharmaceutical Co., Ltd., Osaka, Japan), baby oil (Johnson & Johnson, New Brunswick, NJ, USA), and the water-infiltrated wood marker in the same polypropylene case. All markers are in a polyvinyl alcohol filled phantom container.

QD head coil. Protocols and measurement parameters were as follows and are summarized in Table 1. Protocols included SURVEY: fast field echo; TE 4.6 ms; TR 9.8 ms; flip angle  $15^\circ$ ; scan time 16 s,  $T_1$ WI: spine-echo; TE 10 ms; TR 600 ms; scan time 2 min 56 s,  $T_2$ -weighted imaging ( $T_2$ WI): turbo-spin-echo; TE 100 ms; TR 3000 ms; scan time 2 min 0 s, proton-density-weighted imaging (PDWI): turbo-spin-echo; TE 30 ms; TR 3500 ms; scan time 2 min 30 s,  $T_2^*$ -weighted imaging ( $T_2^*$ WI): fast field echo; TE 9.2 ms; TR 500 ms; flip angle  $25^\circ$ ; scan time 2 min 25 s,  $T_1$ WI spectral pre-saturation with inversion recovery (SPIR): spine-echo;

**Table 1** Imaging parameters

	TE (ms)	TR (ms)	FA ( $^\circ$ )	FOV (mm $\times$ %)	Matrix	Slice thickness (mm)	Slice gap (mm)	Averages	BW (Hz)	Scan time
Survey (FFE)	4.6	9.8	15	250 $\times$ 100	256	10	0	1	124.3	0:16
$T_1$ WI (SE)	10	600	90	170 $\times$ 75	256	4	1	1	163.3	2:56
$T_2$ WI (TSE)	100	3000	90	170 $\times$ 75	256	4	1	3	106.0	2:00
PDWI (TSE)	30	3500	90	170 $\times$ 75	256	4	1	3	289.7	2:30
$T_2^*$ WI (FFE)	9.2	500	25	170 $\times$ 75	256	4	1	2	217.0	2:25
$T_1$ WI SPIR	10	600	90	170 $\times$ 75	256	4	1	1	196.4	3:15
$T_2$ WI SPAIR	100	3000	90	170 $\times$ 75	256	4	1	4	106.0	2:39
PDWI SPAIR	30	3500	90	170 $\times$ 75	256	4	1	4	289.7	2:51
DWI (EPI)	79	5000	90	230 $\times$ 50	160	4	1	3	27.8	2:40
DTI (EPI)	65	5000	90	230 $\times$ 50	128	4	1	2	27.5	3:17

BW, bandwidth; DTI, diffusion tensor imaging; DWI, diffusion-weighted imaging; EPI, echo-planar imaging; FA, flip angle; FFE, fast field-echo; PDWI, proton density-weighted imaging; SE, spin-echo; SPAIR, spectral attenuated inversion recovery; SPIR, spectral pre-saturation inversion recovery;  $T_1$ WI,  $T_1$ -weighted imaging;  $T_2^*$ WI,  $T_2^*$ -weighted imaging;  $T_2$ WI,  $T_2$ -weighted imaging; TSE, turbo spin-echo.

TE 10 ms; TR 600 ms; scan time 3 min 15 s, T<sub>2</sub>WI spectral attenuated inversion recovery (SPAIR): turbo-spin-echo; TE 100 ms; TR 3000 ms; scan time 2 min 39 s, PDWI SPAIR: turbo-spin-echo; TE 30 ms; TR 3500 ms; scan time 2 min 51 s, diffusion weighted imaging (DWI): single-shot echo-planar imaging; *b*-value 0 and 1000 s/mm<sup>2</sup>; three directions; TE 79 ms; TR 5000 ms; scan time 2 min 40 s, and DTI: single-shot echo-planar imaging; *b*-value 0 and 1000 s/mm<sup>2</sup>; 12 directions; TE 65 ms; TR 5000 ms; scan time 3 min 17 s. Default parameters supplied by Philips were used for other parameters and parallel imaging was not used. Phantoms were imaged at the center of transverse to the long axis of the wood marker and syringes. Two images were acquired successively using the same imaging parameters. An apparent diffusion coefficient (ADC) map was calculated from DWI, and a fractional anisotropy (FA) map was calculated from the DTI.

### Analysis

The signal-to-noise ratio (SNR) data were analyzed using ImageJ software (National Institutes of Health, Bethesda, MD, USA) to identify markers on imaging data, according to National Electrical Manufacturers Association standards (NEMA).<sup>8</sup> The image noise was measured using NEMA 2.3.2.1 Method 1. The SNR was measured in all sequences except for ADC and FA map. The SNR of the DWI images was measured using isotropic DWI and by calculating the mean of the three directions in the original images. The SNR of DTI was measured as the mean of 12 directions from the original images. The ADC and FA maps were used to calculate the ADC and FA values.

The coefficient of variation was calculated for each pair of images.

Wood was observed under a microscope to examine its structure. Water that penetrated the wood was sliced using Microtome 3-150-464 (KENIS LIMITED, Osaka, Japan) at a thickness of 3 μm transverse to the wood fiber. The wood test piece was observed on a glass plate. For microscopy, a Motic Microscope BA210LED (SHIMADZU CORPORATION, Kyoto, Japan) with a microscope digital camera system (SHIMADZU CORPORATION) were used.

### Results

Table 2 summarizes the SNRs for various surface markers. The SNRs of MR-SPOTS were ≥52 for all sequences. The SNRs for Breath Care were ≤45 in T<sub>2</sub>\*WI, T<sub>1</sub>WI SPIR, T<sub>2</sub>WI SPAIR, isotropic DWI, original DWI, and original DTI. The SNRs for baby oil were ≤43 in T<sub>2</sub>\*WI, T<sub>1</sub>WI SPIR, T<sub>2</sub>WI SPAIR, isotropic DWI, original DWI, and original DTI. The SNRs for the wood marker were ≥71 for all sequences.

MR-SPOTS had an ADC value of 0.30 mm<sup>2</sup>/s and an FA value of 0.18. The wood marker had an ADC value of 0.96 mm<sup>2</sup>/s and an FA value of 0.80. No signals were observed for Breath Care and baby oil in the ADC map or the FA map.

**Table 2** Signal-to-noise ratio of surface markers

	MR-SPOTS	Breath care	Baby oil	Wood marker
Survey	176	108	412	272
T <sub>1</sub> WI	277	301	287	159
T <sub>2</sub> WI	415	297	325	237
PDWI	435	440	332	281
T <sub>2</sub> *WI	78	45	43	103
T <sub>1</sub> WI SPIR	299	29	34	140
T <sub>2</sub> WI SPAIR	428	7	13	155
PDWI SPAIR	437	150	250	282
DWI (Isotropic)	158	17	31	136
DWI (Original)	104	12	14	80
DTI (Original)	52	10	11	71

baby oil: Johnson & Johnson, New Brunswick, NJ, USA; Breath Care, Breath Care Oral Refreshing Capsule: Kobayashi Pharmaceutical Co., Ltd., Osaka, Japan; DTI, diffusion tensor imaging; DWI, diffusion-weighted imaging; MR-SPOTS, MR-SPOTS Packets: Beekley Medical, Bristol, CT, USA; PDWI, Proton density-weighted imaging; SPAIR, spectral attenuated inversion recovery; SPIR, spectral pre-saturation inversion recovery; T<sub>1</sub>WI, T<sub>1</sub>-weighted imaging; T<sub>2</sub>\*WI, T<sub>2</sub>\*-weighted imaging; T<sub>2</sub>WI, T<sub>2</sub>-weighted imaging; Wood marker, Chamaecyparis obtuse.

Table 3 shows the coefficient of variation for pairs of images. The coefficient of variation of the MR-SPOTS was larger than the coefficient of variation of the other sequences shown in the FA map; the wood marker had similar values in all sequences.

Results of microscopic observations are shown in Fig. 2. Wood tracheids with diameters of 10–30 μm were observed.

### Discussion

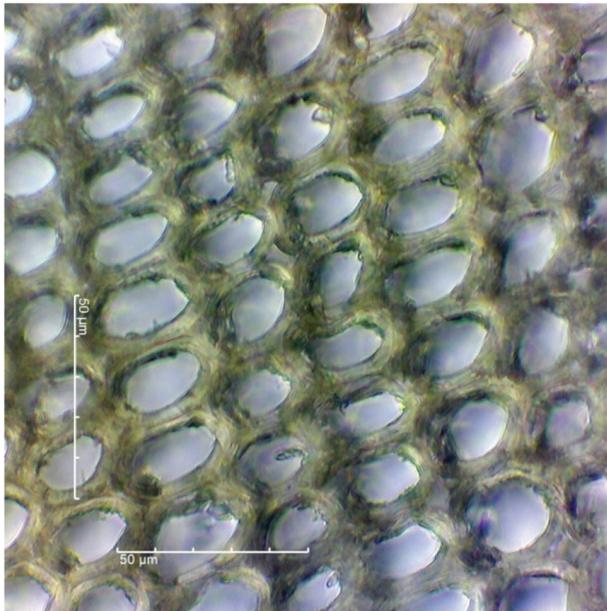
Breath Care (420 ms [pre-study]) and baby oil (240 ms [pre-study]) had short T<sub>1</sub>-relaxation times and high SNR for T<sub>1</sub>WI. However, these T<sub>1</sub>-relaxation times were close to fat (382 ms),<sup>9</sup> and SNR decreased by fat suppression would be difficult to interpret without particularly careful studies. Itoh et al. reported that the SNR of Breath Care and baby oil decrease in fat suppression.<sup>4</sup> The T<sub>1</sub>-relaxation time of the wood marker (708 ms [pre-study]) and MR-SPOTS (651 ms [pre-study]) were longer than that of subcutaneous fat (382 ms), and were less affected by fat suppression.

Because MR-SPOTS are not anisotropic, they had lower FA values than those of the wood marker in the FA map. MR-SPOTS were found to be unsuitable as a marker in the FA map (Fig. 3). MR-SPOTS showed a low ADC value; however, the ADC values for the wood marker were higher than those for the MR-SPOTS in the ADC map. MR-SPOTS were evaluated to be unsuitable as a marker in the ADC map. Additionally, MR-SPOTS, Breath Care, and baby oil produced artifacts in the ADC map (Fig. 4), which required careful interpretation.

**Table 3** Coefficient of variation of surface markers

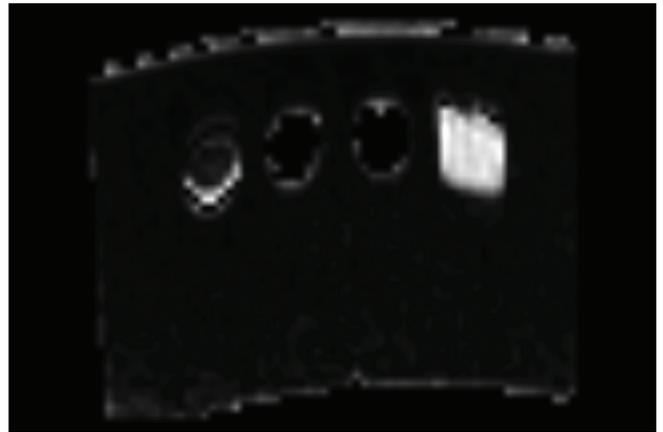
	MR-SPOTS	Breath care	Baby oil	Wood marker
Survey	0.0017	0.0008	0.0014	0.0025
T <sub>1</sub> WI	0.0025	0.0020	0.0025	0.0003
T <sub>2</sub> WI	0.0160	0.0034	0.0039	0.0029
PDWI	0.0013	0.0008	0.0011	0.0017
T <sub>2</sub> *WI	0.0017	0.0029	0.0049	0.0030
T <sub>1</sub> WI SPIR	0.0005	0.0014	0.0039	0.0002
T <sub>2</sub> WI SPAIR	0.0006	0.0636	0.0393	0.0024
PDWI SPAIR	0.0004	0.0023	0.0024	0.0005
DWI (Isotropic)	0.0015	0.0148	0.0105	0.0013
ADC map	0.0140	N/A	N/A	0.0005
FA map	0.0263	N/A	N/A	0.0013

ADC, apparent diffusion coefficient; baby oil: Johnson & Johnson, New Brunswick, NJ, USA; Breath Care, Breath Care Oral Refreshing Capsule: Kobayashi Pharmaceutical Co., Ltd., Osaka, Japan; DWI, diffusion-weighted imaging; FA, fractional anisotropy; MR-SPOTS, MR-SPOTS Packets: Beekley Medical, Bristol, CT, USA; N/A, not available; PAIR, spectral attenuated inversion recovery; PDWI, proton density-weighted imaging; SPIR, spectral pre-saturation inversion recovery; ST<sub>1</sub>WI, T<sub>1</sub>-weighted imaging; T<sub>2</sub>\*WI, T<sub>2</sub>\*-weighted imaging; T<sub>2</sub>WI, T<sub>2</sub>-weighted imaging; Wood marker, *Chamaecyparis obtuse*.



**Fig. 2** The tubular structure of wood observed using an optical microscope. The tracheids are 10–30  $\mu\text{m}$  in diameter.

Different types of wood have variable FA values. FA values of various types of wood were investigated in the pre-study: *Trachycarpus*: FA value 0.1; water content 145%, *Liquidambar styraciflua*: FA value 0.3; water content 138%, *Camellia japonica*: FA value 0.5; water content 120%. The following formula was used to calculate the water content. Water content = mass of water/mass of wood infiltrated with



**Fig. 3** Phantom images in the fractional anisotropy (FA) map of the transverse to the long axis of the wood marker and syringes. The wood marker is clearly visualized in the FA map. Only the wood marker has an FA value that can be used for direct localization in the FA map.



**Fig. 4** The image shows the transverse cross-section of the phantom. Left to right: MR-SPOTS Packets (Beekley Medical, Bristol, CT, USA), Breath Care Oral Refreshing Capsule (Kobayashi Pharmaceutical Co., Ltd., Osaka, Japan), baby oil (Johnson & Johnson, New Brunswick, NJ, USA), and the wood marker. Arrowhead indicates artifacts of MR-SPOTS Packets, Breath Care Oral Refreshing Capsule and baby oil in the image.

water  $\times 100\%$ . The authors recommend *Chamaecyparis obtuse*: FA value 0.8; water content 187%, *Toxicodendron succedaneum*: FA value 0.7; water content 168%, and *Acer*: FA value 0.7; water content 180%. High FA values and high water content are important for wood markers because low water content causes low signal values.

The coefficient of variation of the wood marker was smaller than that of the other marker materials shown in the FA map, and was  $\leq 0.0030$  in all sequences. Values for the wood marker were reproducible compared to those of the other markers for all sequences.

Ghazikhanlou-Sani et al.<sup>10</sup> used Medical Imaging Processing, Analysis, and Visualization (National Institutes of Health, Bethesda, MD, USA) software with T<sub>1</sub> and T<sub>2</sub>. FA maps could be matched with one another, and the tumor

border, soft tissue, and bones could be identified on FA maps. However, the wood marker could be used to directly pinpoint the location of a lesion site on the FA map. Moreover, the proposed marker contributes to lesion localization in many sequences, including fat suppression. Therefore, radiologists may not need to compare the FA map with other images.

Our study had several limitations. Although cost was not determined, a wood marker would be generally inexpensive, and can be constructed by simply infiltrating a piece of wood with water and sealing it with vinyl tape. The cost of the wood marker may be lower than that of commercially available markers. To reduce the cost of essential elements in the clinic, capsule markers have been suggested as substitutes for expensive, commercially available markers.<sup>3,11,12</sup> Rosahl et al.<sup>13</sup> highlighted the excessive cost of commercially available markers and the superiority of shape.

Although the effect of marker shape was not assessed in the present study, a wood marker would be free of shape limitations. Any pressure from a flat marker would not be perceived by a patient. Markers made from wood would enable optimal shape variations, ranging from small to large. Conventional small-capsule markers may be overlooked in large FOV imaging.

Maintaining the quality of a marker was also not studied. However, preventing dryness of the wood marker could be achieved using a polypropylene case that is sealed with vinyl tape. Furthermore, dryness could be prevented by simply dipping the marker in water.

The comparison of markers was performed using phantoms alone. In future studies, the investigation could be extended by imaging human subjects using various markers. Additionally, such studies should include more subject data for various sequences along with comprehensive statistical analysis.

Other materials with known diffusion anisotropy were not considered. Asparagus, which has poor preservability, was excluded. Bundled Dyneema (TOYOBO CO., LTD, Osaka, Japan) was difficult to obtain. Glass plate capillaries were expensive. To make markers widely accessible, materials that were expensive and difficult to obtain were excluded.

## Conclusion

The wood maker was evaluated as useful in DTI, and it enabled direct localization in the FA map. Furthermore, the wood marker yielded sufficient SNRs and coefficients of variation for various sequences. The design and development of a wood marker would be helpful to radiologists and contribute to obtaining useful findings.

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## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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