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This information is current as of June 19, 2025.

*AJNR Am J Neuroradiol* 2008, 29 (9) 1644-1648

doi: <https://doi.org/10.3174/ajnr.A1131>

<http://www.ajnr.org/content/29/9/1644>

# Anomalous J-Modulation Effects on Amino Acids in Clinical 3T MR Spectroscopy

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**SUMMARY:** The signal-intensity loss from anomalous J-modulation effects due to chemical-shift displacement was investigated on amino acid groups (alanine, valine, leucine, and isoleucine) at 3T by using point-resolved  $^1\text{H}$  spectroscopy in patients with brain abscess and phantom experiments. With a larger chemical shift between methyl and methine resonances, alanine shows a greater effect of signal-intensity cancellation compared with other amino acids around 0.9 ppm, resulting in noninverted doublets at a TE of 144 ms.

High-field MR imaging systems such as 3T strength aid in the detection of brain metabolites due to increased sensitivity. However, the clinical 3T system also increases the spatial mismatch of section-selective radio-frequency pulses due to a larger chemical shift difference at higher fields and reduced radio-frequency pulse bandwidths.<sup>1-4</sup> The issue of limited radio-frequency bandwidths is especially prominent with the increasing popularity of parallel imaging with array coils, whose receive-only function demands radio-frequency pulse transmission from the generally inefficient body coil. One frequently encountered challenge of MR spectroscopy at high-field MR imaging systems is the anomalous J-modulation effect on the weakly coupled  $\text{AX}_3$  system, which could hamper identification of the ideally inverted lactate doublet at TE = 144 ms.<sup>1-4</sup>

Although clinical investigations of the anomalous J-modulation effects have centered on lactate<sup>1-4</sup> with theoretic analysis described clearly in a previous article,<sup>5</sup> the possible occurrence arising from other  $\text{AX}_3$  spin systems such as alanine or other amino acids, valine, leucine, and isoleucine, overlaid around 0.9 ppm in brain abscess,<sup>6</sup> to our knowledge, has never been reported. With similar coupling constants exerted on the methyl protons around 7 Hz,<sup>7</sup> these metabolites containing methyl and methine groups also form a lactate-like coupled system with a TE-dependent phase evolution of the methyl resonance. In this study, we aimed to use both in vivo and in vitro experiments to show that the anomalous J-modulation

effect analogous to lactate is also present for alanine, but to a much lesser extent for other amino acids, on a clinical 3T MR imaging scanner.

## Description of Technique and Results

We performed experiments on a 3T scanner (Philips Medical Systems, Best, the Netherlands) using the quadrature body (Q-body) coil for transmission and an 8-channel phased-array modified sensitivity encoding head coil for receiving, by using point-resolved  $^1\text{H}$  spectroscopy sequence (PRESS). The Q-body coil had a maximum transmission B1 field of 13.5  $\mu\text{T}$  ( $\sim 590$  Hz). Single-voxel MR spectral data were obtained with TR/TE = 2000/40, 144, and/or 288 ms with 128 acquisitions (total scanning time, 4 minutes 56 seconds). Two patients with abscesses underwent MR spectroscopic examinations on this system. To investigate the anomalous J-modulation effect on alanine and amino acid groups, we performed in vitro experiments on four 1.5-L bottles of aqueous solution phantom containing 10 mmol/L of alanine, valine, leucine, and isoleucine, respectively. The phantom experiments were performed by using parameters identical to those of the patients, except that the voxel size was fixed at  $25 \times 25 \times 25$  mm<sup>3</sup>.

Figs 1 and 2 show the data from a 19-year-old man and a 42-year-old woman with brain abscess, respectively. The doublet at 1.47 ppm due to the presence of alanine was clearly visible in the 40-ms and 288-ms TE MR spectra (Figs 1B and 2C). However, for the first patient (Fig 1C), there was a positive peak centered on the same resonance which, if from alanine, is expected to exhibit an opposite sign of resonance (ie, inverted doublet) at TE = 144 ms. The spectrum acquired from the second patient with TE = 144 ms (Fig 2B) also exhibited signal-intensity canceling, whereas the spectrum acquired with TE = 288 ms showed substantially larger and clearer alanine resonances than that with TE = 144 ms. The expected inverted doublet of alanine in the 144-ms TE spectra was hardly detectable. Similarly, both of these in vivo spectra also show no clearly identifiable phase inversion of lactate around 1.33 ppm in the TE = 144 ms spectra. In contrast, note that the amino acid groups near 0.9 ppm for the 2 subjects showed clearly inverted spectral lines in the TE = 144 ms spectra without noticeable reduction in signal intensity. The in vivo observations are consistent with results from the phantom experiments, in which an incomplete inverted phase at TE = 144 ms was seen for the

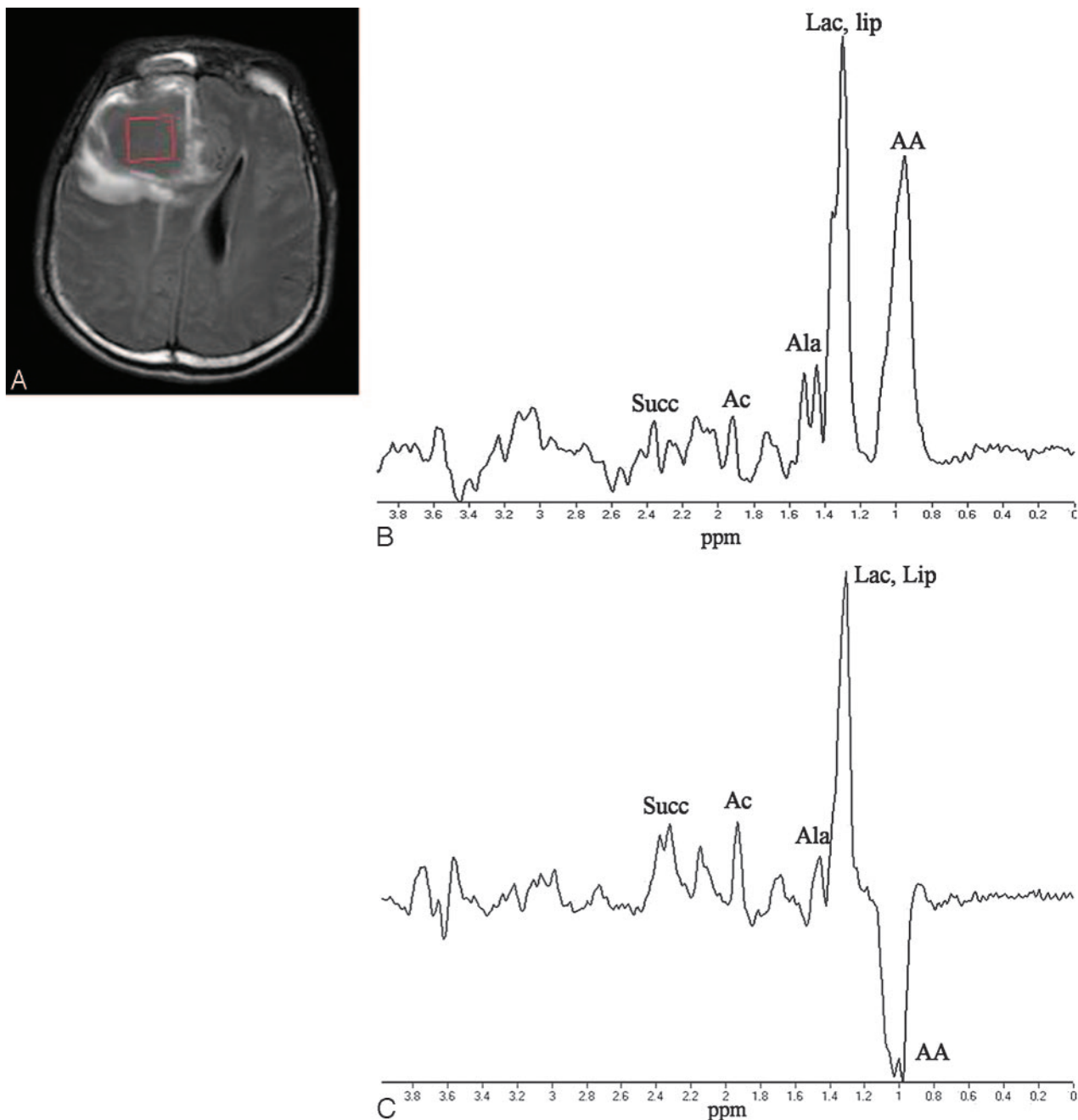
Received September 30, 2007; accepted after revision December 11.

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Supported in part by National Science Council under grants NSC-95-2314-B-002-221-MY3 and NSC-95-2314-B-016-036-MY2.

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DOI 10.3174/ajnr.A1131



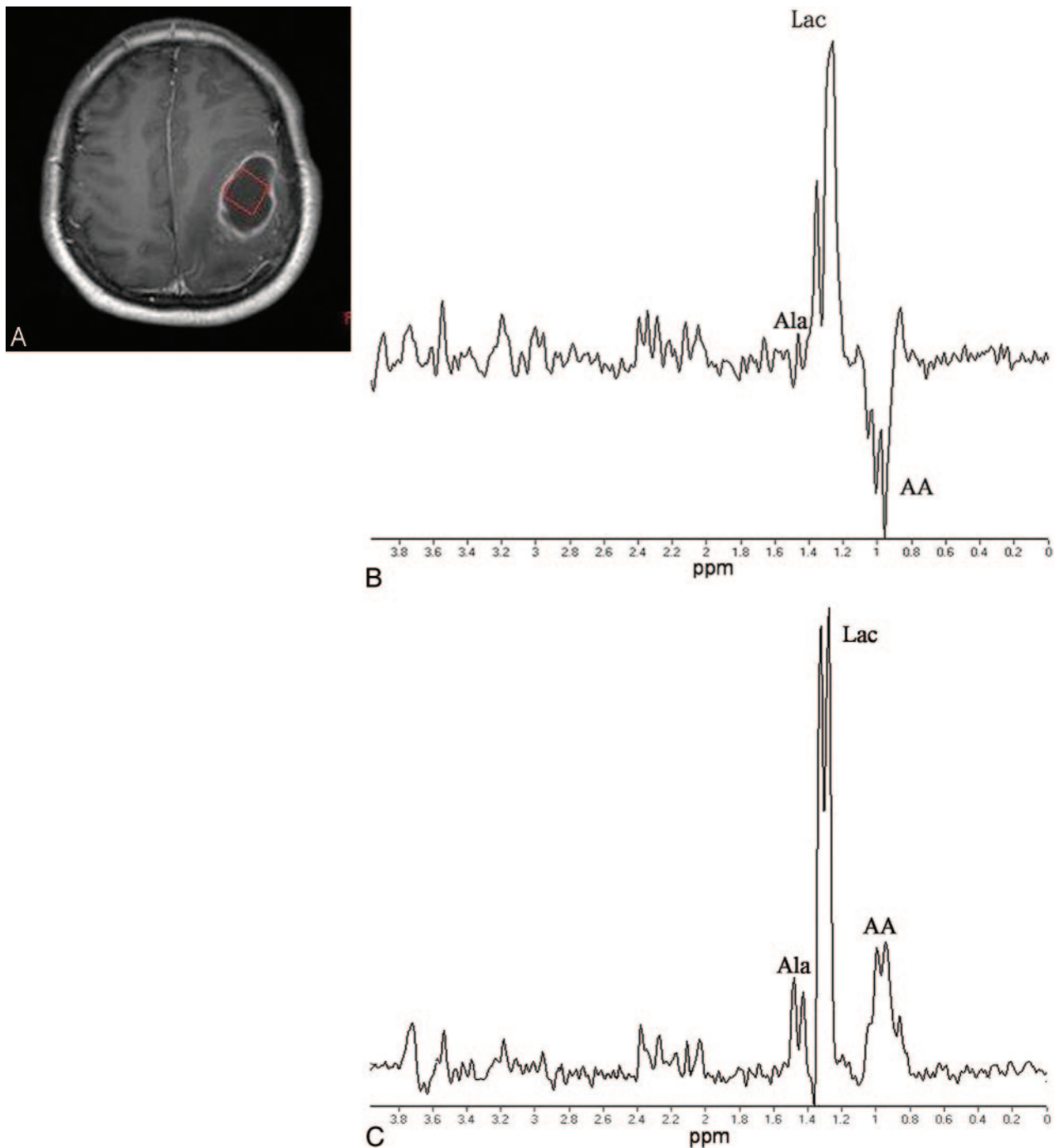
**Fig 1.** Transverse T2 fluid-attenuated inversion recovery MR image (A) and single-voxel spectra obtained in a 19-year-old male patient with brain abscess by using PRESS localization at 3T with TE = 40 ms (B) and TE = 144 ms (C). Succ indicates succinate; Ac, acetate; Ala, alanine; Lac, lactate; Lip, lipids; AA, amino acids.

methyl protons in alanine with reduced amplitude, as opposed to the strong signals in TE = 40 ms and TE = 288 ms spectra (Fig 3), whereas valine (Fig 4), leucine, and isoleucine (not shown) showed clear inverted peaks at TE = 144 ms for the methyl protons with an amplitude comparable with that in TE = 40 ms and TE = 288 ms spectra.

## Discussion

In this study, we demonstrated that the anomalous J-modulation effect analogous to lactate is also present for alanine on a clinical 3T scanner. Our inference suggests that the degree of reduction in sensitivity for alanine detection at TE = 144 ms is similar to that of lactate detection, due to a similar chemical shift difference between the methyl and the methine group

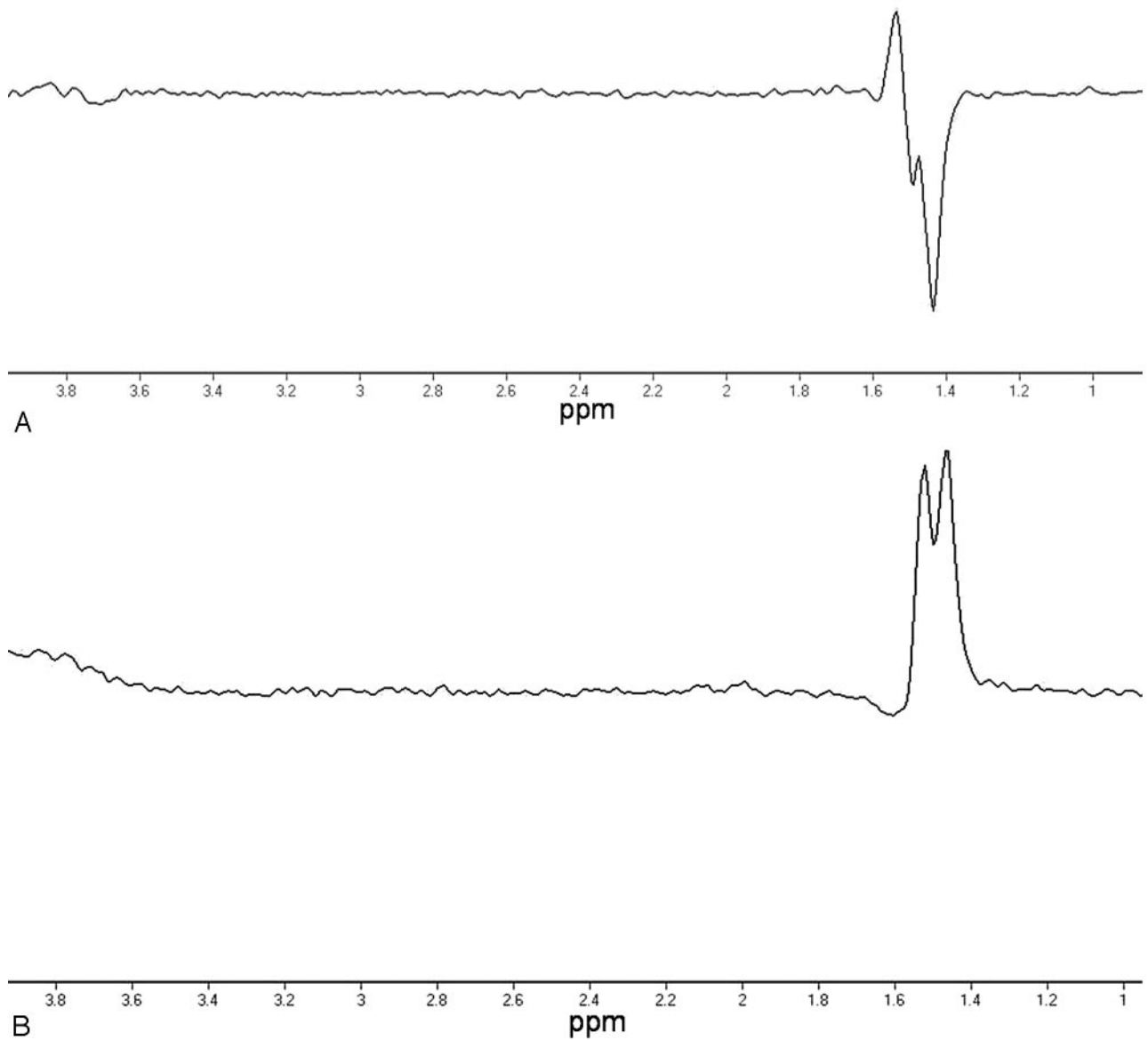
protons (2.78 ppm or 36 Hz at 3T for lactate, and 2.31 ppm or 296 Hz at 3T for alanine, respectively).<sup>7</sup> On our system in which the refocusing radio-frequency bandwidth is 590 Hz, >50% of the methine protons within the section profile may thus exceed the spectral width without experiencing radio-frequency refocusing for each of the two 180° pulses.<sup>3,5</sup> Depending on whether the methine protons within the excitation volume experience the second and/or the third radio-frequency pulses in the PRESS sequence, the excitation volume thus is divided into 4 partial volumes, each with a different phase evolution that leads to destructive interference and consequent signal-intensity loss particularly prominent at TE = 144 ms (1–3, 5).



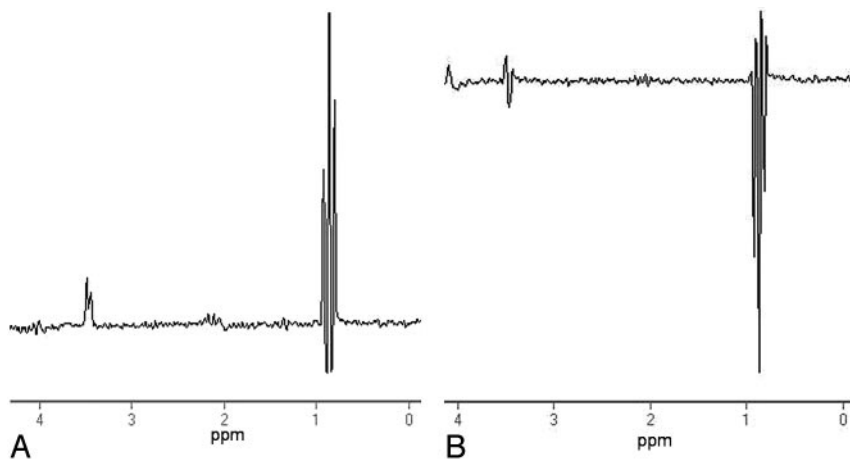
**Fig 2.** Transverse postcontrast T1-weighted MR image (A) and single-voxel proton MR spectra obtained in a 42-year-old female patient with brain abscess by using PRESS localization at 3T with TE = 144 ms (B) and TE = 288 ms (C). Ala, indicates alanine; Lac, lactate; AA, amino acids.

In contrast to the situation of alanine, the chemical shift difference between the methyl and methine resonances is approximately 1.23 ppm (157 Hz at 3T) for valine and 0.70 ppm (89 Hz at 3T) for leucine, respectively,<sup>7</sup> more than a factor of 2 smaller than that found for lactate. Consequently, the signal-intensity cancellation effect is anticipated to be substantially weaker than that for lactate and alanine. In other words, spectra acquired with TE = 144 ms may not show clearly noticeable anomalous J-modulation for the amino acids near the 0.90-ppm region in the spectra, as shown in both our in vivo and in vitro data.

Alanine is potentially a pathologic marker of abscess resulting from bacterial infections of all kinds.<sup>6</sup> It has also been observed following ischemia<sup>8</sup> or in meningioma.<sup>9</sup> Although alanine is not regarded as the most important biomarker for the differential diagnosis between tumor and abscess,<sup>8</sup> a number of animal studies have addressed its potential role in monitoring metabolic alterations following brain injuries.<sup>10,11</sup> Furthermore, the concentration of alanine in the brain, if detectable by in vivo MR spectroscopy, is usually small compared with that of lactate in the presence of prominent anaerobic glycolysis. This means that with destructive signal-inten-



**Fig 3.** Spectra from a phantom that contained 10 mmol/L of alanine to illustrate the anomalous J-modulation effect of the PRESS sequence at TE = 144 ms obtained from a 3T scanner, with the identical setting in the receiver gain at TE = 144 (A) and TE = 288 ms (B). Note at 1.47 ppm the incompletely inverted phase and reduced amplitude of the methyl doublet in the TE = 144 ms spectrum, evidence of the presence of an anomalous J-modulation effect.



**Fig 4.** Spectra from a phantom that contained only valine at TE = 40 ms (A) and TE = 144 ms (B). The complex doublets between 0.90 and 1.06 ppm show a clearly inverted phase at TE = 144 ms.

sity loss due to anomalous J-modulation effects, the identification of alanine at TE = 144 ms by using PRESS is even more prone to error than the situation expected for lactate. Special care in spectral interpretation related to alanine is therefore recommended at high-field systems such as 3T.

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