Contrast-Enhanced Visualization of the Ablation Medium in MR-Monitored Ethanol-Injection Therapy: Safety and Imaging Aspects

D. Nanz[1], J. M. Fröhlich[2], D. Weishaupt[3], K. Treiber[3], S. Ess[4], G. Andreisek[3], T. Pfammatter[3]

[1]Department of Medical Radiology, University Hospital Zürich, Zürich, Switzerland, [2]Guerbet Switzerland, Zürich, Switzerland, [3]Institute of Diagnostic Radiology, University Hospital Zürich, Zürich, Switzerland, [4]Sterile Department, Cantonal Pharmacy Zürich, Zürich, Switzerland

INTRODUCTION

A therapeutic direct delivery of a sclerosing or ablating agent into a lesion is considered an effective treatment for a wide range of pathologies. Absolute ethanol is the most commonly used sclerosing agent[1]. There are a few reports of MR-guided interventions, which exploited the favorable MR image contrast intra-operatively[2-4]. For a reliable identification of the injected ethanol, its conspicuity needs to be improved by a contrast agent. However, there is no published information on the solubility[5, 6] and the molar relaxivity of the gadolinium-based relaxation agents, nor on the rate, with which they dissociate toxic Gd^{3+}, when dissolved in a sclerosing medium. The goals of this study were (1) to estimate the long-term stability of meglumine gadoterate in ethanol/water mixtures and (2) to characterize the spoiled gradient-echo (SPGR) signal at 0.5 and at 1.5 T.

MATERIALS AND METHODS

MR imaging was performed on a 0.5 T intra-operative scanner (Signa SP, General Electric) and on a 1.5 T scanner (CV/i, General Electric). Dilution series of meglumine-gadoterate in 94 % (m/m) ethanol with Gd concentrations from c = 0.5 to 25 mM were prepared. After 6 or 8½ months storage, the amount of free Gd^{3+} in the 6 highest-concentrated samples was determined by direct complexometric EDTA titration, using xylenol orange as endpoint indicator. Pure water, an aqueous gadolinium(III)chloride ($GdCl_3.6H_2O$) solution, and the 500 mM commercialized contrast agent were analyzed in control experiments. The molar relaxivity was measured 6 times over a period of 317 hours (13.2 days) after initial solution preparation. The T_1 relaxation times were determined (fast IR spin-echo, TR/TE 3'000/20 ms, 12 TI times, from 50 to 300 ms) and the relaxivity estimated from a linear regression fit of $1/T_1$ versus c. The signal difference between native muscle tissue and contrast-spiked ethanol was evaluated for SPGR imaging at rates of 1 image/8 s or higher.

RESULTS

In none of the meglumine-gadoterate/ethanol probes could solvated "free" Gd^{3+} be detected. In control experiments, a detection limit of ca. 0.06 mM was estimated. Control experiments also suggested (1) the method to work as expected, and (2) the undiluted aqueous contrast agent to (a) not dissociate Gd^{3+} over months and (b) bind small quantities of free Gd^{3+}. Table 1 summarizes the longitudinal relaxivity values. No temporal trend was identified over 13 days. Figure 1 illustrates the characteristics of the meglumine gadoterate/ethanol versus muscle-tissue signal difference. Theoretical expectations (unbroken lines) were in good agreement with experiment.

Table 1

time/hours	$r_1/(mM^{-1}s^{-1})$	stddev/$(mM^{-1}s^{-1})$
5.0	3.04	0.07
72.5	3.04	0.05
77.5	3.01	0.10
148.5	2.90	0.03
172.5	2.96	0.04
317.5	3.05	0.10

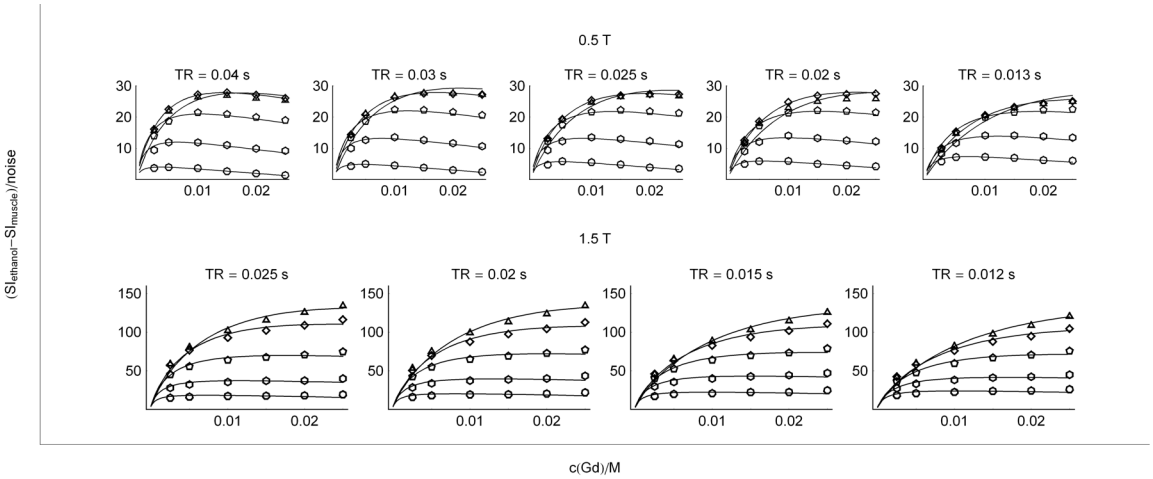

Figure 1 Signal difference between meglumine-gadoterate/ethanol mixtures and muscle-tissue in spoiled gradient-echo images. Results for excitation flip angles 80° (△), 60° (◇), 40° (⬠), 25° (⬡), and 15° (⬡) are shown.

CONCLUSIONS

With an estimated dissociation rate below 0.05%/month, decomplexation of Gd^{3+} ions from the meglumine gadoterate chelate complex dissolved in 94 % (m/m) ethanol does not appear to represent a major risk in MR-guided percutaneous sclerotherapy. The longitudinal molar relaxivities of the contrast agent in ethanolic and aqueous solutions at room temperature and 0.5 T are sufficiently similar to allow the use of standard contrast-enhanced imaging protocols.

REFERENCES

1. Burrows PE, Mason KP. *J Vasc Interv Radiol.* 2004;15:431-445.
2. Lewin JS, Merkle EM, Duerk JL, et al. *Radiology.* 1999;211:566-570.
3. Domb BG, Khanna AJ, Mitchell SE, et al. *Clin Orthop.* 2004;420:225-229.
4. Boll DT, Merkle EM, Lewin JS. *Radiology.* 2004;233:376-384.
5. Wysoki MG, White RI, Jr. *J Vasc Interv Radiol.* 2001;12:264.
6. Friedman MA, Wood BJ. *J Vasc Interv Radiol.* 2003;14:394.