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NMR Evaluation of Stroke in the Rat

R. Nick Bryan,^{1,2} M. Robert Willcott,¹ Nicholas J. Schneiders,¹ and James E. Rose³

Cortical stroke was produced in rats by cautery occlusion of the middle cerebral artery distal to the lenticulostriate origins. Brains were removed, and nuclear magnetic resonance (NMR) scans of whole fixed brains and in vitro measurements of small samples were obtained. Brain tissue was then processed for histology. Routine scans used a modified spin-echo technique. Spin-density and T₂-dependent scans were also obtained. Infarcts were detectable in 6 hr due to diminution of the spin-echo intensity from T₂ prolongation. NMR changes increased gradually over 48 hr and coincided anatomically with evidence from the neuropathologic sections. NMR imaging is a very sensitive method of evaluating acute cerebral infarction in this animal model.

Nuclear magnetic resonance (NMR) has demonstrated important imaging capabilities for neuroradiology. In the case of stroke, the limited number of published cases already suggest advantages over computed tomography (CT) [1-4]. However, the specific NMR appearance of stroke remains unclear. This is because of incomplete data on the alterations in spin density and T₁ and T₂ relaxation times produced by ischemia and the technique-dependent mingling of these NMR variables to produce an image. Thus, an infarct may appear black or white in comparison with normal brain, depending on the pulse sequence used.

The purpose of this study was to develop an imaging technique that allows quantification of individual pixel NMR parameters, particularly spin density and T₂. The technique was then applied to surgically infarcted rats in order to determine NMR changes.

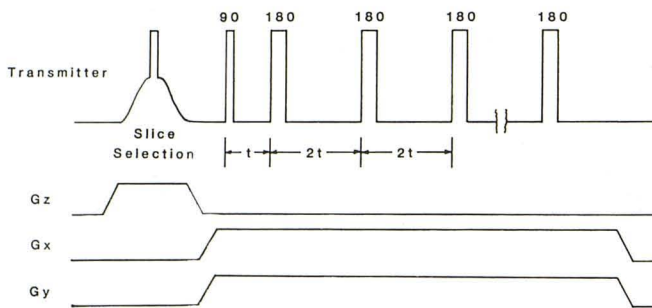
Materials and Methods

Under general anesthesia, cortical stroke was produced in 12 rats by cautery occlusion of the middle cerebral artery distal to the lenticulostriate origins. Animals were sacrificed by intracardial formalin perfusion at 1 hr, 12 hr, 24 hr, 48 hr, 14 days, or 30 days postinfarction. The fixed brains were removed for imaging.

A 200 MHz Mini-Imager (Bruker Instruments, West Germany) was used. This unit has a basic imaging technique of projection-reconstruction, with selective excitation for slice determination. The data acquisition pulse sequence is a modified Carr-Purcell-Meiboom-Gill spin-echo train with a 90° excitation pulse followed by a train of 180° read pulses. The number of 180° pulses can be varied, but in most of our experiments 16 were used (fig. 1A). Since all echo measurements were made with the X-Y gradient field on, each echo contains spatial information and may be treated as free-induction decay and Fourier transformed to a projection. In addition, the logarithm of the amplitude of the spin echoes is a function of T₂ and may be used to determine this number.

In most cases, four consecutive spin echoes were summed to create each of a series of four images (fig. 2A). This improves the signal-to-noise ratio while still providing sufficient data for T₂ measurements. The earliest image has good anatomic detail, little noise, and is primarily a function of spin density. The later images show less anatomic detail due to greater noise from diminishing signal, but are primarily a function of T₂ (particularly longer T₂ regions).

While useful, this image display does not provide the desired quantification. However, if the Bloch equations are applied to a Carr-Purcell-Meiboom-Gill sequence and solved for spin density



$$S_j = \frac{1}{n} S_0 \sum_{i=0}^{n-1} e^{-(tj+it)/T_2}$$

$$\ln S_j = -\frac{1}{T_2} t j + \ln \left[\underbrace{\frac{1}{n} S_0 \sum_{i=0}^{n-1} e^{-it/T_2}}_B \right]$$

slope A

y-intercept B

thus

$$T_2 = - \frac{1}{A} \frac{e^B}{e^B}$$

$$S_0 = \frac{1}{n} \sum_{i=0}^{n-1} e^{-it/T_2}$$

Fig. 1.—A, Modified Carr-Purcell-Meiboom-Gill NMR pulse and gradient sequences for spin-echo data acquisition. B, Basic formulas for obtaining spin density and T₂ from summed spin echoes in this sequence.

A

B

¹ Department of Radiology, Baylor College of Medicine, Houston, TX 77030.

² Department of Radiology, Methodist Hospital, Mail Station NB703, 6565 Fannin, Houston, TX 77030. Address reprint requests to R. N. Bryan.

³ Department of Neurosurgery, Baylor College of Medicine, Houston, TX 77030.

Fig. 2.—Normal rat brain. **A**, Initial series of spin-echo images. Data from first four echoes at upper left; data from last four echoes at lower right. **B**, Calculated spin-density image. **C**, Calculated T_2 image.

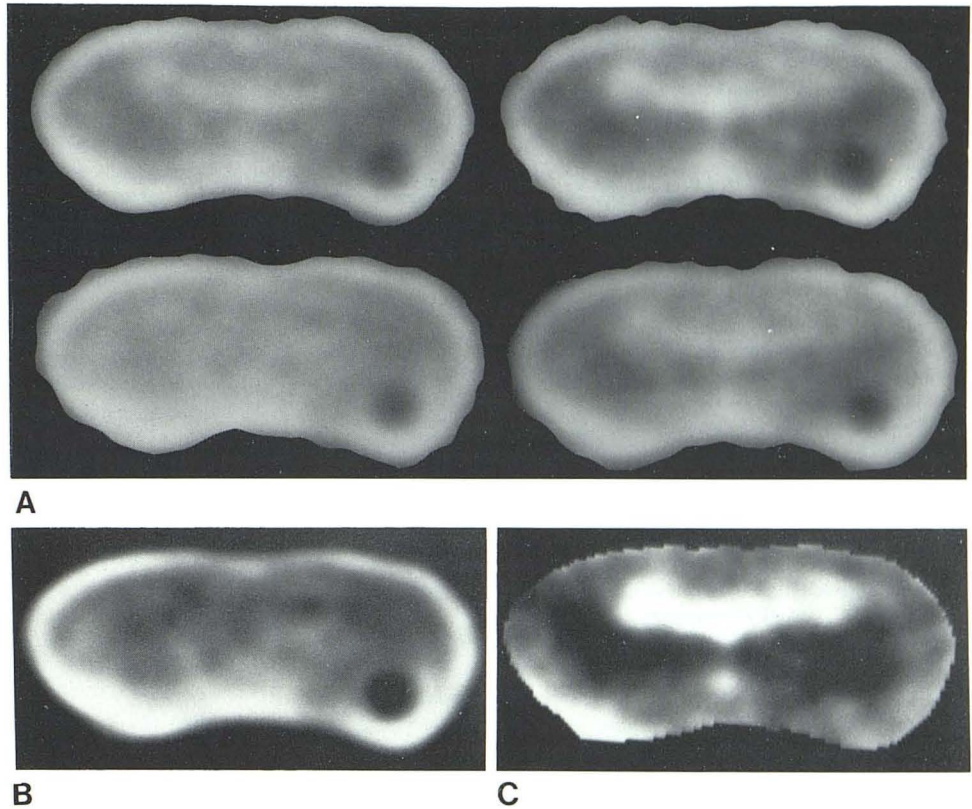
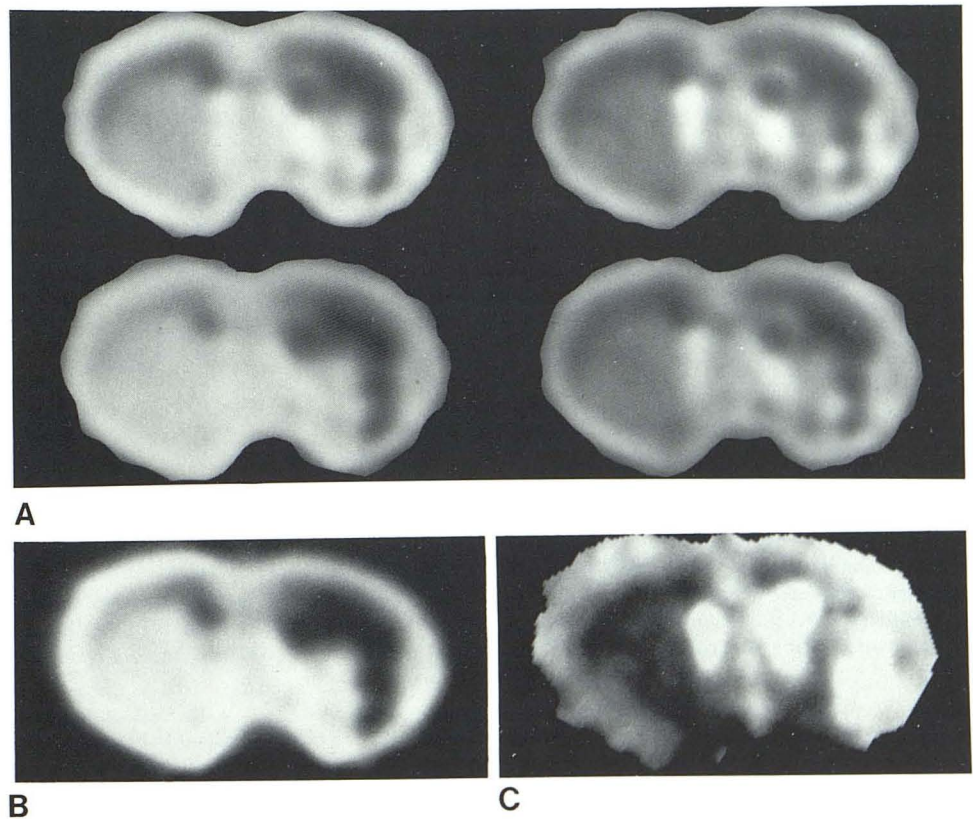


Fig. 3.—Rat brain 28 days after central left ganglionic infarction. **A**, Initial series of spin-echo images. Decreased signal intensity in region of stroke. **B**, Calculated spin-density image. Decreased signal intensity in region of stroke. **C**, Calculated T_2 image. Increased signal intensity in stroke from prolonged T_2 .



and T_2 , a semilog plot of measured signal intensity yields spin density as a function of the Y intercept and T_2 by the slope of the fitted line for each pixel (fig. 1B), since each spin-echo image pixel is a direct function of signal intensity. By applying this technique to the original scan data, it is possible to create one image that is a function of spin density and another that is a "true" T_2 image (figs. 2B and 2C, respectively). T_2 measurements calculated in this manner have less than 10% error probability as determined by phantom testing.

Results

All surgically infarcted animals except those imaged at 1 hr postinfarction had demonstrable infarcts on NMR scans. The earliest imaged strokes were detectable at 6 hr postinfarction. In all cases, the infarcts appeared as areas of generally decreased NMR signal intensity. This was noticeable on the original spin-echo scans and calculated spin-density images. This is probably due either to diminished hydrogen-1 content, or, more likely, to a T_1 component from partial saturation. In addition, all infarcts had prolonged T_2 values as indicated on calculated T_2 images. A typical example is shown in figure 3. This animal was imaged at 28 days postinfarction. The sequence of spin-echo images reveals an overall decrease in signal intensity in the region of the stroke (fig. 3A). The calculated T_2 image (fig. 3C) clearly shows an increase in T_2 values (about 80 msec in the stroke compared with 35 msec for normal tissue). These T_2 values can be read on the gray scale. At present, the data are statistically inadequate to correlate NMR parameters with time elapsed after infarction.

Discussion

The eventual clinical value of NMR in the evaluation of cerebral stroke will depend on two factors: (1) its sensitivity in detecting lesions, particularly in the acute phase, when other techniques such as CT are of limited diagnostic value; and (2) the specificity of the

results. This specificity will most likely depend on accurate documentation of the intrinsic NMR parameters, spin density, T_1 and T_2 , in stroke as in other diseases. The results of our animal experiments, like previous animal and human studies [1, 4], suggest the sensitivity of NMR in detecting early stroke is superior to that of other current imaging modalities. Preliminary results suggest ischemic regions of the brain may be demonstrable by NMR as early as 6 hr after the ictal event, and perhaps earlier in some cases. The specificity of the changes in the intrinsic NMR parameters remains a research problem. The NMR technique reported here provides relatively accurate quantification of spin density and T_2 , but no quantification of T_1 . Our results confirm that T_2 is prolonged in stroke, as suggested by others [1]. However, this and similar techniques must be applied to other disease processes in order to determine specificity of the T_2 alterations. Such work is in progress.

In summary, pixel spin-density and T_2 measurements can be determined by using a modified Carr-Purcell-Meiboom-Gill spin-echo technique to create spin-density and T_2 images. Application of this technique to animal data indicates that T_2 is prolonged in stroke.

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