Simulation Procedure to Determine Nuclear Magnetic Resonance Imaging Pulse Sequence Parameters for Optimal Tissue Contrast

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In order to permit a more optimized selection of acquisition parameters for nuclear magnetic resonance (NMR) imaging a simulation procedure is proposed to determine the pulse sequences for optimal tissue contrast for a variety of clinical indications. In selected patient studies an adequate set of source images is measured, which allows computation of images of all possible pulse sequences, and measurement of tissue contrast within selected regions of interest. Data concerning promising sequences for specific clinical indications can then be filed, so as to aid the investigator's experience in setting up future NMR acquisitions.

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In the present-day practice of nuclear magnetic resonance (NMR) imaging the acquisition parameters (spin-echo or inversion recovery mode, echo times, repetition times, inversion times) are set, prior to the measurement, in a more or less arbitrary manner. Usually the pulse sequences applied are the result of the investigator's experience, or of studies in the literature concerning the particular clinical indication. Often a series of measurements is made, each with different acquisition parameter settings, in the hopes that one will be optimum. In order to reduce the number of acquisitions necessary, and to improve the target to nontarget contrast associated with the abnormality or tissue of interest, we propose a procedure by which the selection of optimal acquisition parameters for a range of clinical indications can be improved. The method is based on the fact that once the proton density (N_H), spin-lattice (T_1) and spin-spin relaxation time (T_2) images of a tomographic slice are known, this information is sufficient to be able to accurately compute ("simulate") the images associated with all possible acquisition pulse sequences (*1*). N_H, T_1, and T_2 images can be computed from a combined multidelay inversion recovery (IR) and multiple spin-echo (SE) acquisition (*2,3*).

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This paper describes the proposed simulation procedure, illustrated by two clinical examples of its application.

MATERIALS AND METHODS

T_1, T_2, and N_H images were computed from patient data produced with IR and SE pulse sequences. Typically, eight images of each particular object slice were generated, four from IR with inversion times ranging from 33 to 3,000 msec, and four echo images from a single SE with an echo time of 52 msec. The imaging frequency was 21.4 MHz, slice thickness 10 mm, and signals were averaged over two acquisitions. The images were arranged into 128 × 128 arrays of 32-bit real numbers. This is also the format in all the computations described below. Pixel-by-pixel computation of T_1, T_2, and N_H values was carried out by evaluation of the Bloch equations corresponding to the pulse sequences applied, as we described in previous papers (*3,4*). Usually the tissue structure of interest could already be observed in one or more of the measured or computed images. A region of interest (ROI) r_o was drawn manually to indicate its location, as well as ROIs (r_i, i = 1 . . n) for the surrounding tissue, one for each region observed to be approximately uniform, adjacent to r_o (Fig. 1). On the basis of the N_H, T_1, and T_2-values of all pixels within these regions, SE and IR signal-values were computed for each individual pixel, for ~250,000 simulated pulse sequences. The acquisition time parameters were permutations of ranges of inversion (TI), echo (TE), and repetition times

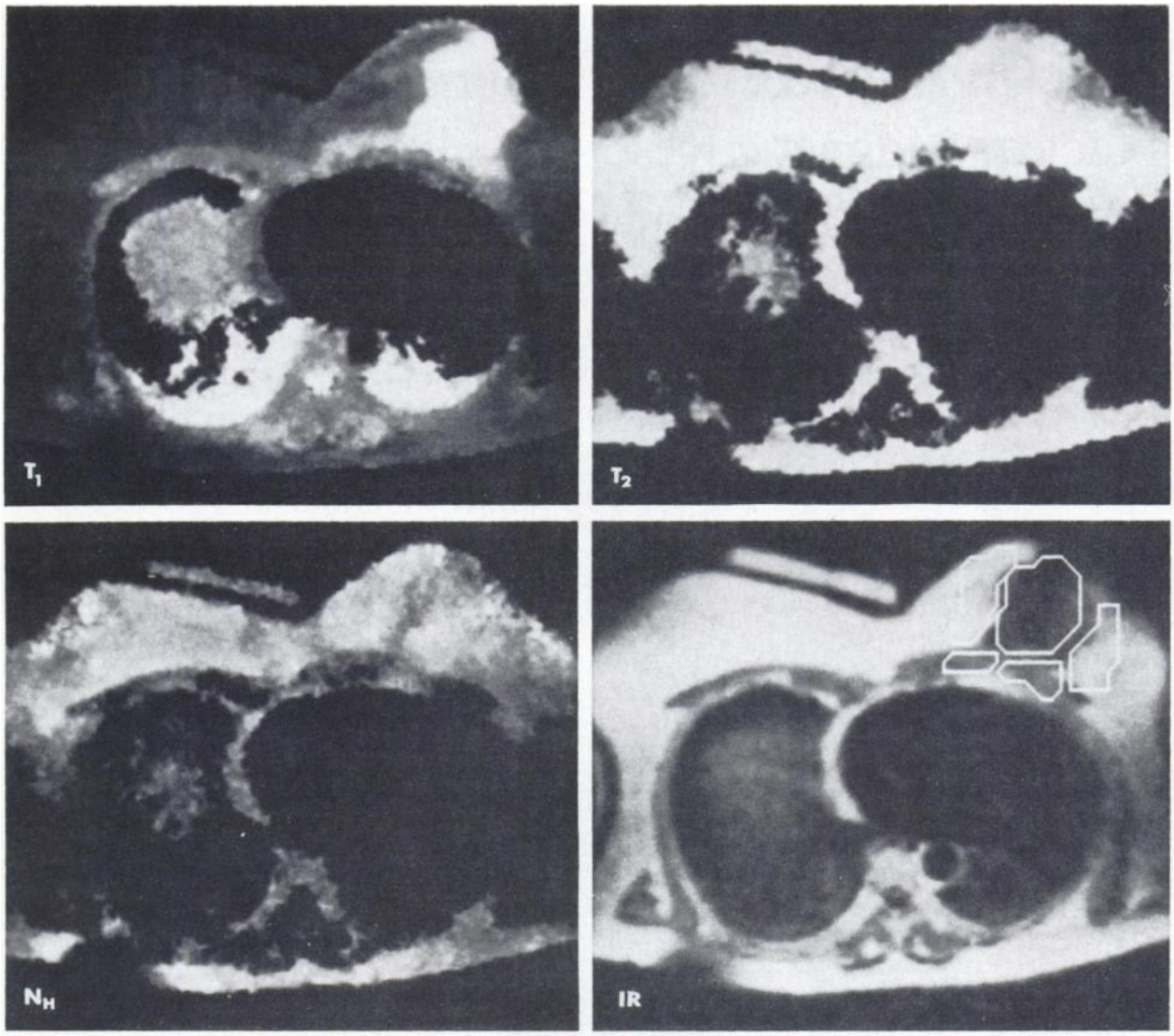

FIGURE 1
Computed images T_1, T_2 and N_H of patient suffering from tumor in left breast, and (measured) IR image in which ROI r_o is drawn over tumor, surrounded by four background ROIs r_1-r_4. Flat object over right breast is calibration wedge used for purposes beyond scope of this paper. Notice that in computed images, pixel values that originate from SE and IR signals below a certain threshold have been set to zero (*3*)

(TR) within appropriate limits for actual patient imaging (10-1,000, 2-120, and 20-3,500 msec, respectively).

For each of these simulated experiments a contrast to noise ratio (CNR) for r_o with respect to its surroundings r_i, $i = 1 \ldots n$ was computed as the smallest of the CNR_i-values for all r_o-r_i pairs. CNR_i is computed by a scheme (*5*) that takes signal value, signal noise, and total scan time into account (see Discussion).

For each of the different inversion times applied in the simulation study a "contrast map" was created as an image in which the X-coordinates are echo times, the Y-coordinates are repetition times, and each pixel value is the CNR that was computed for its corresponding TI/TE/TR combination (Fig. 2). These contrast maps were inspected visually, and were scanned to find the (optimal) pulse sequence TI/TE/TR that corresponded to the highest CNR. For several pulse sequences, both SE and IR simulated images were computed on the basis of N_H, T_1, and T_2 images, by applying the appropriate Bloch equations. Among these images was the one corresponding to the optimal pulse sequence (Fig. 3). In order to validate the optimization method, some simulated images (Fig. 4) were computed corresponding to the pulse sequences that had actually been utilized in the corresponding patient study. Measured and computed images, as well as related contrast maps, were filed for future consultation.

DISCUSSION

The N_H, T_1, and T_2 images were computed from four IR and four SE images. One may compute these from only three independent images (e.g., one IR and two SE), although doing so shortens the duration of the acquisition, degrades the quality of the computed im-

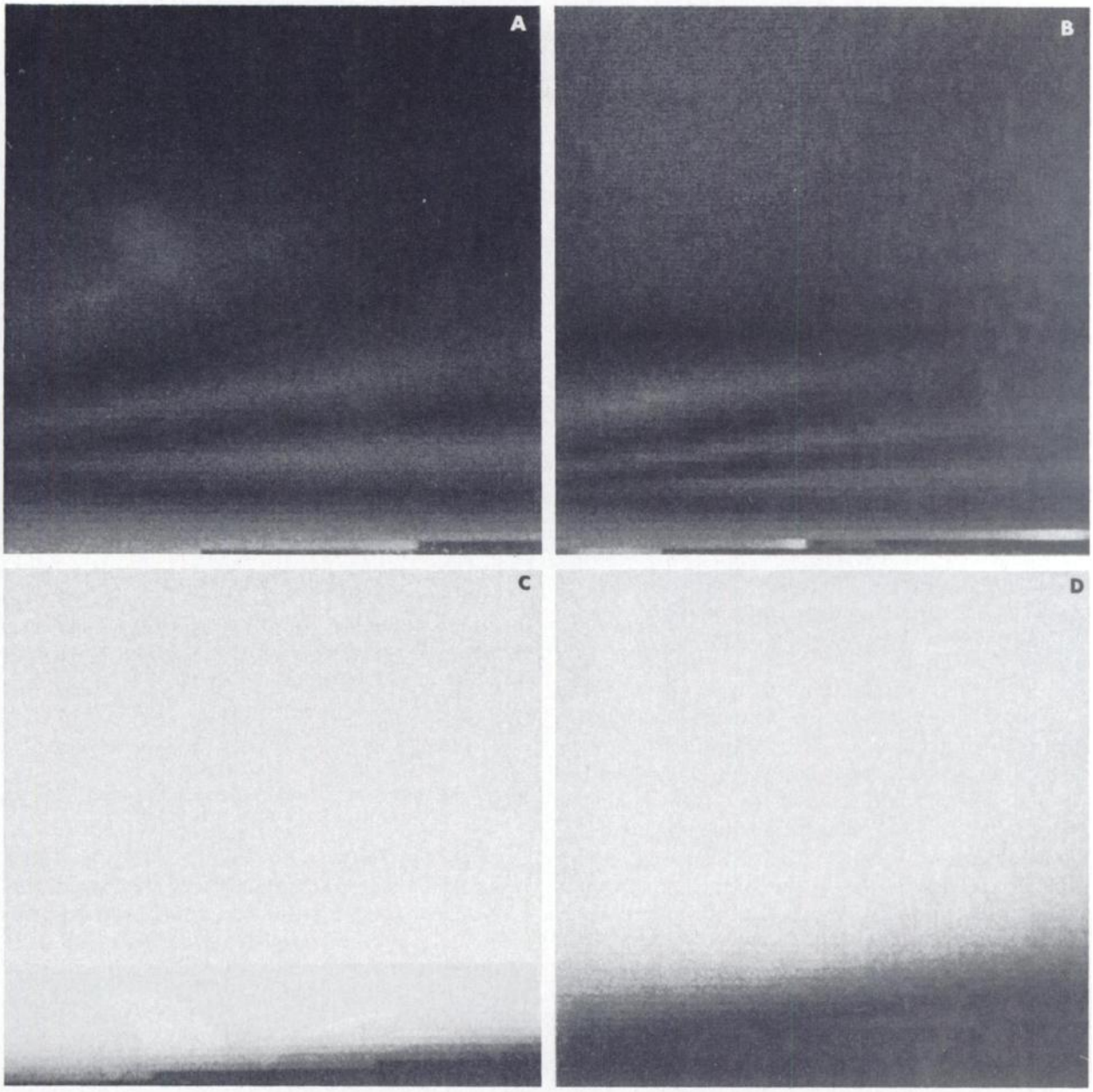

FIGURE 2
Some of contrast maps computed from data in Fig. 1. A: SE; B: IR with TI = 20 msec; C: IR with TI = 160 msec; D: IR with TI = 400 msec. In each of four maps, horizontal coordinates (from left to right) are TE values ranging from 2 to 128 msec, vertical coordinates (from bottom to top) are TR values ranging from 50 to 3,200 msec. TI = 160 map (C) contains very highest CNR value, at TE = 18 msec and TR = 1,800 msec

ages, and, hence, the uncertainty of the final optimum pulse sequence is increased (*6,7*). A trade-off can be established only on the basis of a larger number of studies than we have performed.

In our experiments, we restricted ourselves to the simulation of images, corresponding to simple SE and IR pulse sequences. However, the simulation procedure can also be applied to arbitrary pulse sequences, e.g., more complicated ones, or sequences that are promising but difficult to carry out with the current hardware.

Drawing ROIs may lead to problems typical of many quantitative in vivo nuclear medicine studies; for example, whether variations within a ROI are systematic or due to statistical noise. The central and leftmost (to the observer) ROIs in Fig. 5A may or may not together cover a uniform area of carcinogeneous tissue. In fact Fig. 5B demonstrates that a simulation experiment designed to optimize the contrast of the central ROI alone against its surroundings yields a difference. It should be noted, however, that in such cases it may be advisable to perform an actual measurement with the optimal pulse sequence computed.

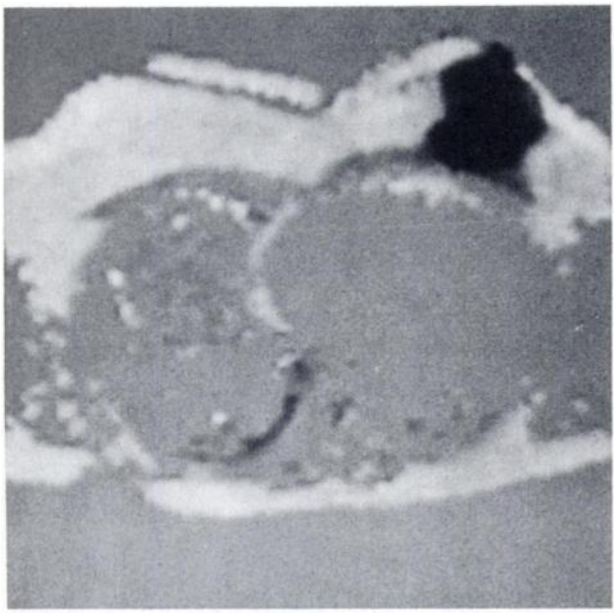

FIGURE 3
Image, computed from N_H, T_1, and T_2 images in Fig. 1, simulating optimal pulse sequence for particular patient study: IR measurement with TI = 160 msec, TE = 18 msec, and TR = 1,800 msec

Another problem concerns physical phenomena, such as flow, that cannot (or only with great difficulty) be incorporated into the equations used to model the NMR measurement. Figure 6 shows that the simulated image fails to match the corresponding measured image in areas where tissues or substances have moved during the course of the measurement. Extreme care should be taken to leave these structures out of tissue and background ROIs, and a checking procedure (such as creating the images of Fig. 6 for the study of Fig. 5) should always be performed.

The scheme that is applied for computing CNR_i as a contrast measure for a ROI r_o against a ROI r_i deserves special attention. We used Edelstein's differential signal to noise ratio (*5*) to compute CNR_i:

$$DSNR_i = \frac{|S_o - S_i|}{\sigma}\left(\frac{TS}{TR}\right)^{1/2} = \frac{\Delta S}{\sigma}\left(\frac{TS}{TR}\right)^{1/2}, \quad (1)$$

in which S is the average signal in a ROI, σ is the noise in the bandwidth locally in the image, and TS is the total imaging time. We did not, however, set $\sigma = 1$, since we did not want to exclude noise from other than pure instrumental sources (e.g., variations in tissue characteristics within an ROI) and since we suspected that, given a fixed TI/TE/TR, the signal noise is not invariant to the biochemical variations throughout the image. We set TS/TR to an arbitrary constant (TS/TR = 1), since we assumed multislice data collections where the desire to keep TR short in order to increase the number of repetitions are offset by the need for long TR values in order to collect multiple slices. Therefore, our CNR formula becomes:

$$CNR_i = \frac{\Delta S}{\sigma}, \quad (2)$$

in which σ is computed as the standard deviation of ΔS:

$$\sigma = (\sigma_o^2 + \sigma_i^2)^{1/2}, \quad (3)$$

in which σ_o and σ_i are the standard deviations of S_o and S_i. Notice that the expression in Eq. (2) also describes

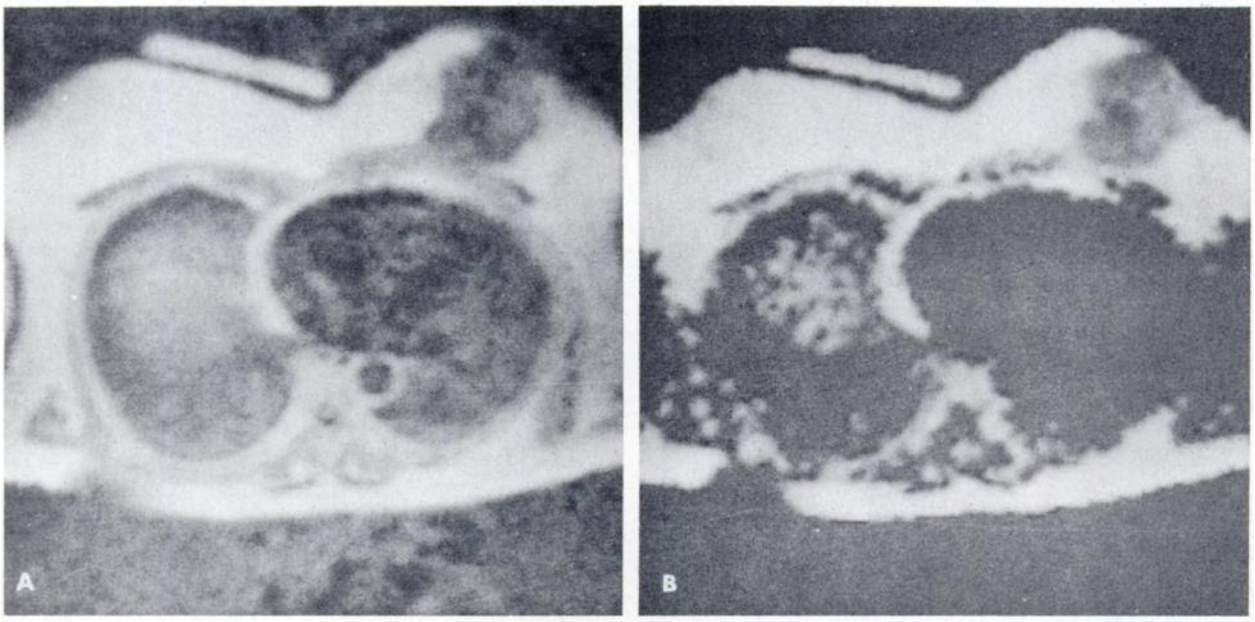

FIGURE 4
A: IR image, measured with pulse sequence of TI = 500 msec, TE = 52 msec, and TR = 1,526 msec. B: Computed image for same pulse sequence

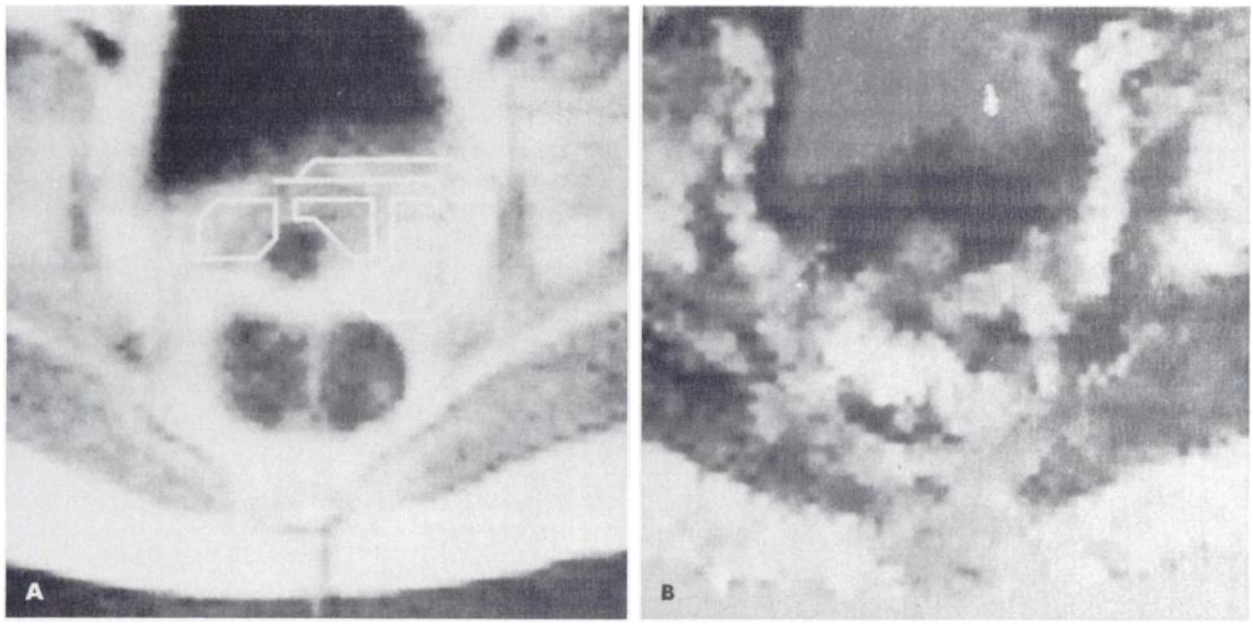

FIGURE 5
A: Measured IR image of patient suffering from cervix uterus carcinoma. Large black structure in upper part is bladder. Circular dark object in middle is vagina, containing applicator with calibration substance. Tumor is dark gray kidney-shaped area (see also Fig. 6) adjacent to vagina, over which two of four ROIs are drawn. B: Computed optimal contrast image with respect to central ROI in A, simulating IR measurement with TI = 71 msec, TE = 4 msec, and TR = 206 msec. Note difference of areas left and right of applicator, adjacent to bladder

the visual discernability of two adjacent image regions. In the case where single-slice data collection is to be simulated, the CNR formula becomes equal to Eq. (1). Finally, we assumed that the noise in computed images resulted from normal propagation of errors in the calculations, and was proportional to the noise in measured images (*1*,*8*).

Interestingly, CNR, as a measure of contrast, performed better than DSNR (with $\sigma = 1$) when the images computed for optimal contrast were visually compared. This is illustrated in Figs. 3 and 4B, where the pulse sequence applied in the latter is almost identical to the optimal sequence of TI = 480, TE = 58, TR = 1,600, which resulted from a simulation study by using

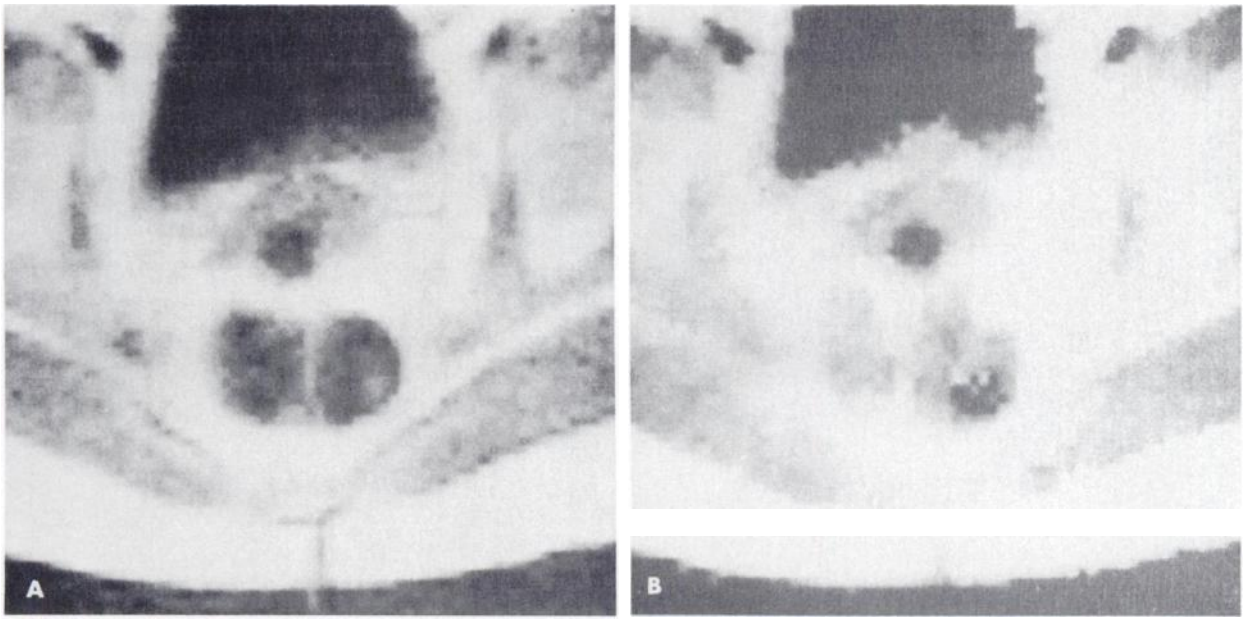

FIGURE 6
A: IR image of patient of Fig. 5, measured with TI = 500, TE = 52, TR = 1,526 pulse sequence. B: Simulated image, computed with same pulse sequence. Note different appearance of rectum (split dark area dorsal to vagina in A)

DSNR as a contrast measure.

As has been shown before with respect to simulated images obtained from SE studies (*2*), the optimal acquisition parameters found by a simulation study may be unattractive in a practical sense, due to the duration of the acquisition involved, or to machine limitations. Although the chance of unattractive schemes is reduced when IR sequences are also produced, in the selection of clinically optimal acquisition schemes produced by the simulation procedure one must carefully balance high contrast with practical considerations.

As compared to simulation studies based on phantoms or NMR parameters obtained in other manners, the above-described method deals with biologic tissue in its in vivo environment, and with actual clinical indications. The simulation procedure proposed here is meant to create, in the course of performing routine patient studies, a learning file to assist the investigator in setting up future NMR acquisitions, and in doing so comprehensively add knowledge to his/her experience.

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