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NUCLEAR MAGNETIC RESONANCE IMAGING OF HUMAN LYMPH NODES

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ABSTRACT

MR-imaging of surgically excised enlarged and non-enlarged human lymph nodes was studied in patients with and without malignant metastatic lymphadenopathy. NMR tomograms were performed at frequency of 200 MHz using the CPMG sequence. Space resolution was up to 0.1mm. "In vitro" NMR-tomograms of both non-enlarged and enlarged lymph nodes disclosed tiny foci of metastatic deposits. It is proposed that use of T_2 differences for localization of a pathologic focus is an effective mode of visualization during NMR tomography at high frequency.

Nuclear magnetic resonance (NMR) has demonstrated important imaging capabilities for normal and abnormal structures of the central nervous system, thorax, abdomen, pelvis, and muscular skeletal systems. The contrast resolution of NMR in differentiating soft tissues is decidedly superior to that of computer tomography (CT) and derives from differences in proton density and T_1 and T_2 relaxation times. In imaging lymph nodes, a limited experience also suggests advantages over CT, but to date, clinical NMR imaging has failed to detect small metastatic deposits in normal-sized lymph nodes (1-3).

Sensitivity and specificity of NMR appearance of lymphadenopathy also is unclear, probably because of incomplete data on the alterations in spin density and T_1 and T_2 relaxation times produced by metastases and the technique-dependent mingling of these NMR variables in producing an image. Thus, a metastatic deposit in a lymph node may appear black or white in comparison with surrounding soft tissue, depending on the pulse sequence used. It is still unclear which parameter or combination of parameters is the most sensitive discriminator for this diagnostic goal. Therefore, it is not as yet possible to choose the optimal imaging technique from among the many available.

The purpose of this study was to develop an imaging technique that allows differentiation of small metastatic deposits from normal lymphoid tissue. The technique was then applied to surgically removed nodal specimens in order to determine NMR changes in the normal-sized lymph node.

MATERIALS AND METHODS

We obtained NMR tomograms of 32 lymph nodes removed at operation in 11 patients (age 41 to 56 years). Three male patients had lung carcinoma and female patients had thyroid cancer (2 patients), breast cancer (4 patients), and skin melanoma (2 patients). The size of the examined lymph nodes varied from 0.5 to 6.0cm. The NMR equipment used was a mini-imaging system (Bruker Instruments,

Fig. 1: NMR tomogram of two normal lymph nodes from the hilum of the lung.

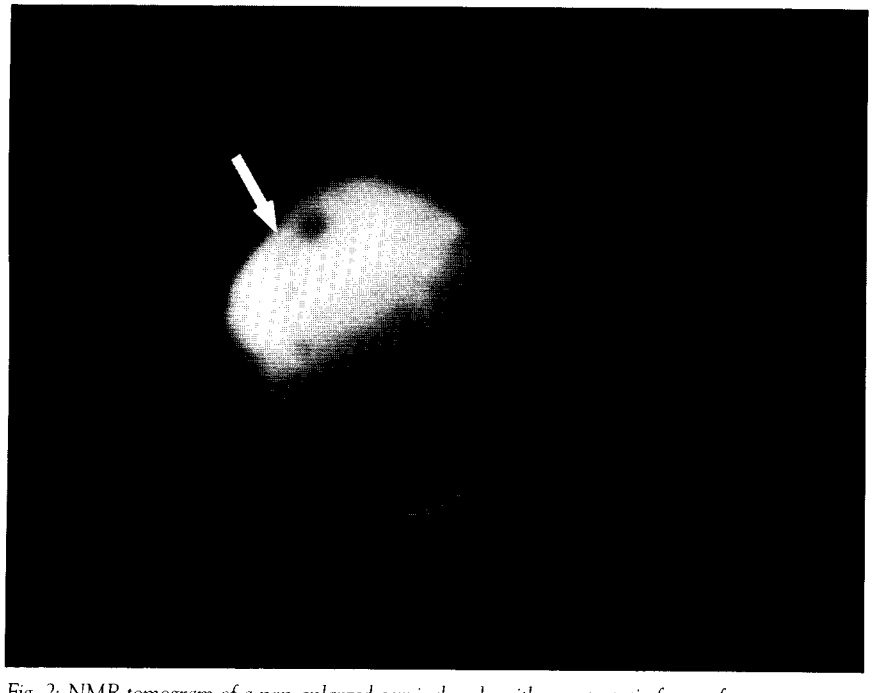

Fig. 2: NMR tomogram of a non-enlarged cervical node with a metastatic focus of melanoma. The metastasis corresponds to an area of increased signal intensity (arrow).

Rheinstethen, West Germany), which consisted of a 90-mm-diam bore superconducting magnet fitted with gradient coils, 30 mm H' probe head, and modified CXP spectrometer console. The magnet was operated at 4.7 T corresponding to a proton resonant frequency of 200 MHz. The pulse sequence used was a modification of the Carr-Parcell-Meiboom-Gill (CPMG) technique. Excitation and detection was achieved by 90° pulse followed by train of 32 180° pulses spaced at 7.5ms. Each 180° pulse generated a spin-echo that represents a projection trough that selected 1mm-thick slice as determined by applied x and y gradients. One hundred twenty sets of echoes were collected, sampling projections at intervals of 1.5° and covering a total of 180° about the lymph node. The total time for the scan was approximately 10 min. High resolution 256 pixel square image was reconstructed via standard convolution-filtered back projection, giving an element resolution that measured 0.1 × 0.1 × 1.0mm.

In most examinations, 8 consecutive spin-echoes are summed to create each of a series of 4 images. This technique improves the signal/noise ratio. The earliest image has little noise and is primarily a function of spin density. Later images show greater noise from diminishing signal, but are primarily a function of T_2 (particularly longer T_2 regions). NMR signals are displayed on gray scale. The structures having the highest signal intensity (short T_1, long T_2) appear white, while those with the least signal density long T_1, short T_2) appear black. To improve the image of metastatic lesions and to differentiate them more clearly from normal nodal structures, we used image reconstruction of different groups of echo signals obtained in CPMG sequence.

RESULTS

Fig. 1 shows the tomograms of two normal lymph nodes of the lung hilum. A rounded formation in the cortical substance and longitudinal one in the medulla are visible. In this image, a relatively homogenous structure of unaffected lymph nodes is not followed by an increase in T_1 and T_2 values (i.e., there are no significant differences in intensity of NMR signals from normal parenchyma).

A notably different pattern is seen in a non-enlarged lymph node (8mm diam) partially replaced by tumor. *Fig. 2* shows the NMR image of a cervical lymph node with metastatic melanoma deposit. The affected area differs considerably from that in the normal parenchyma on T_2 parameter. An increased NMR signal makes differences between the abnormal tumor and normal tissue areas more visible.

With complete metastatic nodal replacement *(Fig. 3)*, the bright zones predominate as T_2 increases. No normal lymphoid tissue is visualized, a finding confirmed by histologic examination.

The results of image reconstruction analysis using CPMG sequence are shown in *Fig. 4* (four images of a cervical lymph node containing malignant thyroid deposits). The first image depends primarily upon proton density. The signal intensity from the metastatic focus and adjacent fluid-filled cysts are approximately equal and differentiation of these lesions is not possible. By increasing the dependence of signal intensity on T_2 parameter, the contrast of the metastases and cysts both progressively increase and reach a maximum at an NMR image obtained by summarizing the last 8 spin echo signals. Not only the cyst wall but also the metastatic structure is defined.

DISCUSSION

Earlier reports (1,3,4) described low-field NMR-imaging (up to 0.35 T) in patients with CT-proven lymphadenopathy. Abnormal lymph nodes were identified by an increased size and other morphological changes and not by tissue characteristics established by signal intensity information.

Mann et al (5) obtained low-field NMR images of two surgical specimens and detected metastatic deposits in lymph nodes smaller than 2cm in diameter. Ordinarily such small foci are not detectable by computerized tomography. Although it was hoped that NMR could distinguish non-enlarged (normal) lymph nodes from those

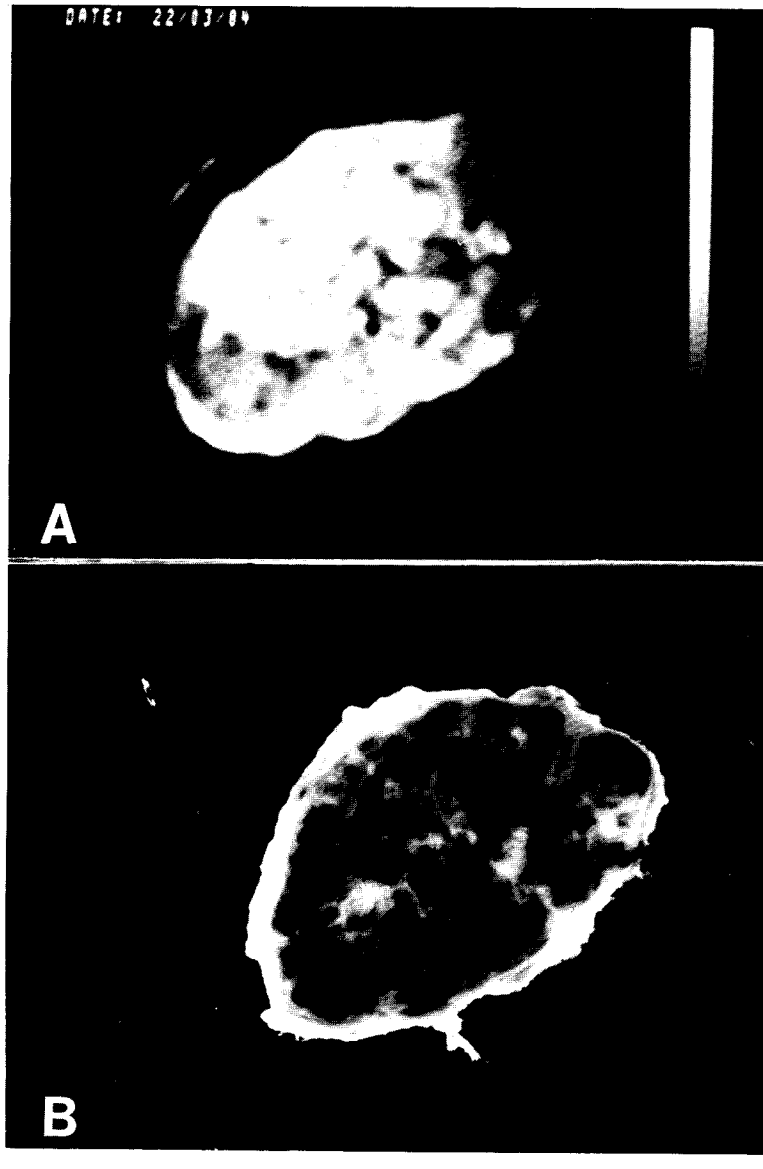

Fig. 3: a) NMR tomogram of cervical lymph node completely replaced by metastatic melanoma. b) Photograph of the same lymph node in section.

partially replaced by tumor, this differentiation has not been found possible for resistive NMR imaging systems. This "failure" is explainable by low anatomic resolving power of NMR imaging devices that depend upon spatial resolution, contrast between different tissues, and the signal-to-noise ratio of these tissues. Although low-field NMR using appropriate pulse sequence offers better contrast sensitivity than CT, both spatial resolution and signal-to-noise ratio are inferior to those of CT. In this regard, our study suggests that NMR imaging at high magnetic field has distinct advantages over low-field NMR. The increased signal-to-noise ratio permits thinner sec-

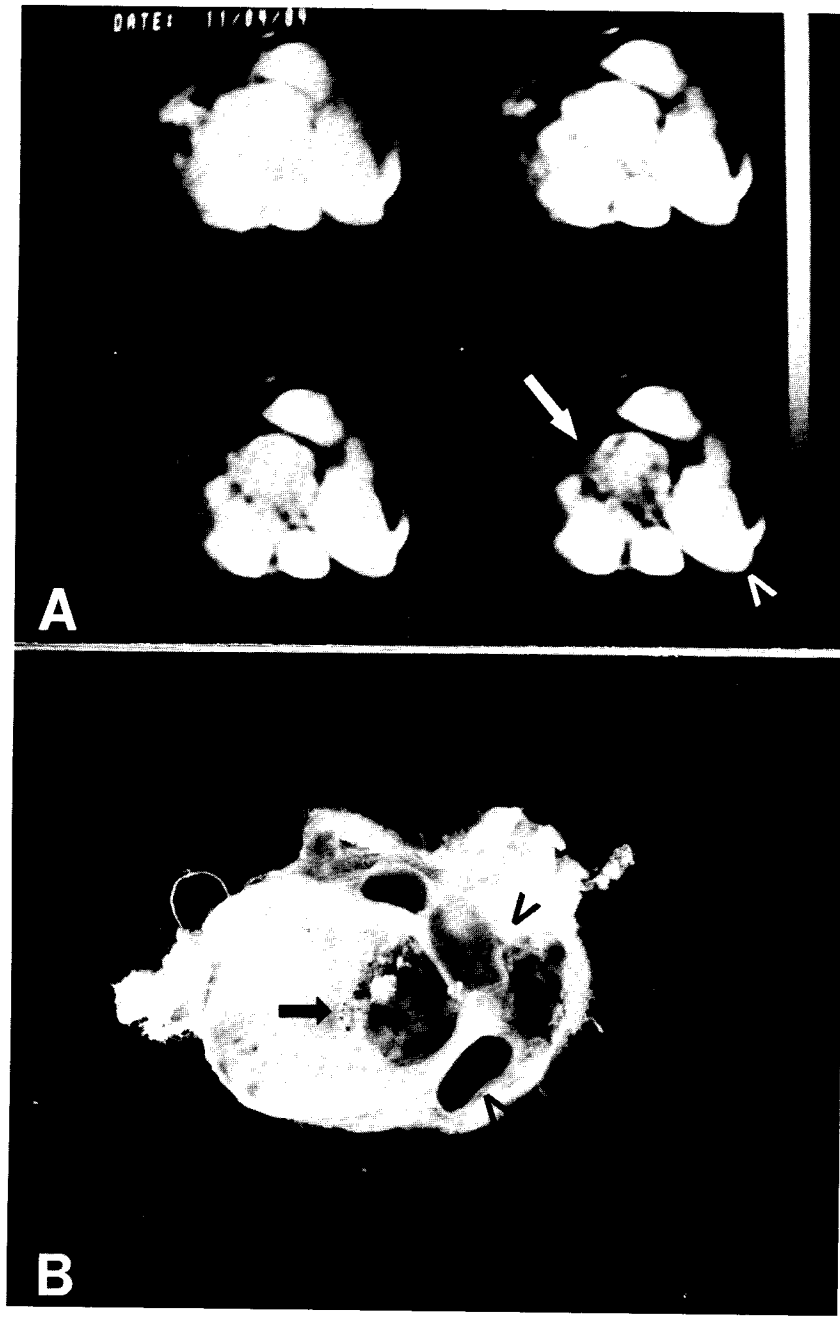

Fig. 4: a) NMR tomogram of a cervical lymph node with a central metastasis from thyroid cancer. The image was reconstructed by a summation of 8 echo signals of protons in the layer undergoing study. Tumor (arrow) emits a low-intensity signal relative to that of cysts (arrowhead). b) Photograph of a gross preparation of the same lymph node. There is striking similarity in the morphology and spatial distribution of metastasis (arrow) and cysts (arrowheads) between the gross specimen and NMR image.

tioning and improves the spatial resolution without prolonging scan time excessively. The images obtained at high magnetic field strength reveal both the anatomic structure and abnormality of the lymph node in greater detail than that obtained using low-field resistive and superconductive systems. Our investigation also corroborates theoretically predicted and experimentally verified improvements in both signal-to-noise and contrast-to-noise ratios in NMR imaging when field strength is increased (6,7) and we were able to delineate extremely small metastases in non-enlarged lymph nodes.

At the current investigational stage of NMR clinical imaging, however, a sufficient data base is lacking (i.e., reliable relaxation and density parameters have not been determined at the high-field strength (up to 4T)). An alternative approach is to establish scan protocols in such a manner that sufficient number of images are obtained, encompassing a broad range of settings of the pulse timing parameters for each coordinate and section of lymph nodes. As for T_2, the CPMG sequence satisfies these criteria. In this manner at least one of the images is assured close to contrast optimum for metastases in lymph nodes, and further, it enables computation of T_2. Indeed, this relaxation time may be a highly important parameter for metastatic detection at high-field NMR. Our studies support the findings of Kroeker et al (8) who favor the use of high frequencies for T_2-dependent imaging sequences for early tumor diagnosis.

The limitations inherent to these scan protocols are self-evident. A single parameter like T_2 does not uniquely characterize lymph nodes. Moreover, neither T_1 nor proton density can be derived from scan protocol delineated by our study. Clearly augmenting the number of descriptors from 1 (T_2) to 3 (T_1, T_2, proton density) increases the likelihood for clustering, but this technique still needs to be applied to other diseased lymph nodes to determine the overall specificity of metastatic appearance with NMR.

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