Quantitative assessment of pulmonary edema by nuclear magnetic resonance methods

Antonio G. Cutillo, MD, Alan H. Morris, MD, David C. Ailion, PhD, Carl H. Durney, PhD, and Krishnamurthy Ganesan, PhD

Considerable progress has been made in the application of nuclear magnetic resonance (NMR) imaging and nonimaging techniques to the quantitative assessment of pulmonary edema. NMR measurements offer the advantages of being noninvasive, relatively rapid, and easily repeatable. In addition, NMR imaging is suitable for the determination of lung water distribution. Studies of various animal models have shown that NMR techniques can adequately detect and quantify relative changes in lung water content and distribution in various types of experimental lung injury. Preliminary observations in humans suggest that NMR measurement of relative lung water changes in clinical pulmonary edema should be feasible. Although the application of NMR to the assessment of pulmonary edema appears to be very promising, it also poses significant problems that must be solved before it can be established as a standard experimental and clinical method.

INTRODUCTION

The importance of pulmonary edema in experimental and clinical medicine justifies the extensive efforts that have been made to develop and apply methods for quantifying the accumulation of lung water. However, the methods that have been developed so far have technical limitations that substantially reduce their sensitivity and accuracy, as well as their practical applicability.[1–7] Because of its accuracy, the long-established gravimetric technique remains the reference standard in lung water research, although its destructiveness is a serious disadvantage that precludes its use in clinical investigations. None of the available methods meets all of the criteria for optimal clinical measurement of lung water: accuracy and reproducibility, high sensitivity, noninvasiveness, practicality, low cost, no hazard to the patient, and the ability to provide regional information.[6,7] The chest radiograph[6–9] is the sole widely accepted approach to the clinical assessment of lung water accumulation, although other methods (thermal-dye dilution technique, soluble inert gas technique) may find application under specific conditions.[6,7]

The above limitations may be substantially improved by new approaches, among which the application of nuclear magnetic resonance (NMR) techniques appears to be particularly promising. NMR lung water measurements offer the advantages of being noninvasive, relatively rapid, and easily repeatable. In addition, NMR imaging is particularly suitable for the determination of lung water distribution. Because of these attractive features, various NMR techniques have been tested in animal models of pulmonary edema; only a few observations have been made to date in humans. Although the available data are still not conclusive, they clearly demonstrate the potential of NMR as a means of detecting and monitoring pulmonary edema. However, these studies have also shown significant problems that must be solved before the NMR approach can be established as a standard experimental and clinical method.

This article will briefly review published data on the application of NMR techniques (particularly NMR imaging) to the study of pulmonary edema. The NMR determination of lung water content and distribution has been discussed in greater detail in a previous issue of the *Journal of Thoracic Imaging*,[5] of which this article is an update.

QUANTITATION OF LUNG WATER FROM NMR DATA

Although nuclei other than protons (eg, sodium) are

AGC: Division of Respiratory, Critical Care, and Occupational Pulmonary Medicine, University of Utah Medical Center, Salt Lake City, Utah; AHM: Pulmonary Division, LDS Hospital, Salt Lake City, Utah; DCA: Department of Physics, University of Utah, Salt Lake City, Utah; CHD: Department of Electrical Engineering, University of Utah, Salt Lake City, Utah; KG: Department of Physics, University of Utah, Salt Lake City, Utah. Reprints: A.G. Cutillo, Division of Respiratory, Critical Care, and Occupational Pulmonary Medicine, University of Utah Medical Center, 50 N Medical Dr, Salt Lake City, UT 84132.

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NMR-sensitive, proton NMR techniques have generally been used for lung water studies since protons are present in the body in much greater concentrations. Therefore, the term "NMR" in this article will refer to proton NMR unless otherwise specified. The basic principles of proton NMR are extensively discussed in a number of publications.[10–16] Lung water content can be determined from the intensity of the proton NMR signal, which is directly proportional to the concentration of hydrogen nuclei (proton density) and therefore to the concentration of water in the specimen.[10–16] Under appropriate technical conditions, the NMR signal defines the absolute water concentration. However, a number of causes of signal loss can interfere with the accurate quantitation of lung water by NMR. Immediately following a radiofrequency magnetic field pulse, the NMR signal intensity decays with time because of the dephasing of the precessing protons due to magnetic field inhomogeneity. In a perfectly homogeneous external magnetic field, this decay (free induction decay) would be characterized by the time constant T_2 (the transverse, or spin-spin, relaxation time). T_2 thus quantifies the irreversible loss of signal due to inhomogeneity in internal local magnetic fields. External (magnet-induced) field inhomogeneity further increases the signal loss and results in a shorter free induction decay (expressed by the time constant T_2^*). This extra loss of signal is recovered when NMR spin-echo techniques are employed. In addition, a reversible NMR signal loss due to internal (sample-induced) magnetic field inhomogeneity has recently been observed in inflated lungs.[17–19] This signal loss results in an even shorter free induction decay (characterized by T_2'), as discussed below.

The rate of longitudinal recovery of nuclear magnetization (the reestablishment of equilibrium magnetization along the externally applied magnetic field direction) after a radiofrequency pulse is characterized by the relaxation time T_1 (the longitudinal, or spin-lattice, relaxation time). In order to allow complete longitudinal recovery of nuclear magnetization, the repetition time—the time between the beginning of one pulse sequence and the beginning of the next identical pulse sequence—must greatly exceed the T_1 value for the specimen.

Although the dependence of the NMR signal intensity on T_1 and T_2 is frequently exploited in NMR imaging to enhance tissue differentiation, this dependence complicates the quantitation of absolute lung water content.

NMR LUNG WATER STUDIES IN NORMAL AND EDEMATOUS LUNGS

Relaxation times

Studies based on various experimental animal models have demonstrated that NMR techniques can detect and quantify pulmonary edema. Lauterbur and associates[20,21] showed that lung T_1 was increased in dogs with pulmonary edema induced by steam inhalation. These investigators[20] demonstrated a relationship between T_1 and gravimetric lung water content and proposed the use of NMR techniques to quantify lung water accumulation. The relationship between T_1 and lung water content in excised lungs and living animals has been confirmed in other experimental models of both increased permeability and hydrostatic pulmonary edema induced in various animals (dogs, rabbits, rats, and mice) by injection of oleic acid[22–24] or alloxan,[25] saline infusion,[23] endotracheal saline lavage,[26] or inflation of an aortic balloon and saline infusion.[24] Lanir and Gilboa[27] and Shioya and coworkers[28] studied the time course of the T_1 changes in living mice and rats exposed to high oxygen concentrations; Shioya and coworkers[28] correlated these changes with gravimetric, bronchoalveolar lavage, and histologic data and found an increase in T_1 associated with water accumulation (during the acute stage of the injury). Lung T_2 has also been observed to increase in experimental pulmonary edema[22–26,28] and has been found to correlate well with gravimetric lung water content.[22,23,25,26,28]

Relative water content

Using an NMR imaging spin-echo technique, Hayes and associates[29] quantified lung water content from the intensity of the NMR signal and were able to detect regional pulmonary edema simulated in excised rat lungs and in intact (dead) rats by intrabronchial saline instillation. These and other investigators have measured NMR signal intensity (also by imaging techniques) in excised lungs or in vivo to quantify and monitor pulmonary edema induced in sheep by inflation of a left atrial balloon[30] and in rats by oleic acid injection[22,23,31] or rapid saline infusion.[23,31] They have found a good agreement between NMR signal intensity and gravimetric lung water content.[22,23,29,31]

Siefkin and Nichols[32] recently quantified lung water accumulation in various rabbit models of pulmonary edema by measuring the area under the proton NMR spectra obtained by topical NMR (in which the signal was detected by a surface coil); they observed a good correlation between changes in spectral area and gravimetric results.

Lung water distribution

Several investigators have shown the remarkable potential of NMR imaging for assessing water distribution in normal and edematous lungs. A study of excised rat lungs demonstrated the accuracy of this approach (as indicated by the good correlation between regional NMR and gravimetric data) and the excellent spatial resolution achievable by NMR imaging (which could detect differences in water content between lung tissue slices with volumes of as little as 0.075 mL).[33] Carrol et al[30] and Wexler et al[26] quantified the

spatial distribution of water by measuring relatively large lung regions (eg, upper lung v lower lung) in sheep and dogs (normal and with pulmonary edema induced by inflation of a left atrial balloon or by endotracheal lavage). NMR imaging clearly demonstrated the effect of gravity on lung water distribution in these studies.

In addition to the conventional topographic (spatial) approach to the study of lung water distribution, a new, nonspatial method has recently been proposed that uses NMR imaging data to generate a distribution of fractional lung volume (V_f) as a function of lung water density (ρH_2O).[31] An analysis of this distribution provides the average ρH_2O and a quantitative measure of the inequality of lung water distribution. Studies in excised rat lungs and in living rats have shown that pulmonary edema induced by oleic acid injection or rapid saline injection is associated with marked changes in the V_f v ρH_2O distribution. These changes reflect both the increased lung water content and, in the case of the oleic acid model, the marked spatial inequality of the injury. The average ρH_2O correlated well with gravimetric lung water content.[31] The V_f v ρH_2O distribution method has been used successfully in rats to follow the time course of experimental lung injury.[31]

Human studies

Published data regarding the application of NMR techniques to the study of pulmonary edema in humans are still very sparse. Johnston and associates[34] studied normal and abnormal excised human lungs and demonstrated an increased NMR signal intensity in edematous lungs. T_1 measurements in excised edematous lungs[34] and in living subjects with pulmonary edema[35] showed no consistent changes, although the T_1 value was high in at least one patient.[35] Other studies have been confined to normal subjects. Using NMR imaging, several investigators[30,36,37] have demonstrated regional differences in the NMR signal reflecting the effects of gravity on the distribution of lung water. A preliminary V_f v ρH_2O distribution, as described above, has been obtained from normal subjects.[38] The results of these studies, as well as those of nonquantitative NMR imaging of the chest,[39] suggest that NMR imaging can be used to study pulmonary edema in humans, although some limitations and problems need to be specifically addressed.

Absolute lung water content

The data obtained from experimental animals and humans provide firm evidence that NMR imaging and nonimaging techniques can detect and quantify lung water changes associated with pulmonary edema. However, in most published studies, the NMR data (NMR signal intensity and relaxation times T_1 and T_2) have been used as relative measures of lung water content. Few attempts, with varied results, have been made to derive the absolute lung water content from the basic NMR measurements. In one study,[33] regional and overall absolute lung water content was determined from excised rat lung specimens using an NMR line-scan imaging technique; no systematic difference was found between NMR and gravimetric measurements. In contrast, in another study,[37] determinations of absolute lung water content by a planar ("spin-warp") imaging technique in excised sheep lungs underestimated gravimetric lung water content by about 20%. Furthermore, lung water measurements performed by the same NMR technique in human subjects were also significantly lower than values predicted from data in the literature.[37] The discrepancy between these two studies likely reflects the effects of technical factors.[5,37] Compared with the measurement of relative lung water changes, the determination of absolute lung water content has more stringent technical requirements that, if not met, significantly limit the accuracy of the data.

Nonproton NMR lung water measurements

Although proton NMR was used to obtain all the experimental data discussed above, it is not the only possible NMR approach to measuring lung water. Combined sodium and proton imaging has recently been used to assess lung water in rats with pulmonary edema induced by the administration of alloxan or saline.[40] In this study, a correlation was observed between sodium NMR data and total or extravascular gravimetric lung water content. The sodium NMR approach is of particular interest for the discrimination between intravascular and extravascular lung water compartments but is still at a preliminary stage of development.

COMBINED RELAXATION TIMES AND PROTON DENSITY MEASUREMENTS

As indicated by the literature, relaxation time and proton density measurements have generally been used individually as measures of lung water content. Recent studies,[23,25,35,41] however, suggest the interesting possibility that T_1 and T_2 measurements may complement the proton density data, thus providing a more comprehensive assessment of lung water and pulmonary edema. According to these studies, the determination of T_1 (and/or T_2) in addition to proton density might be valuable in differentiating lung edema from other causes of increased proton density (eg, vascular congestion or atelectasis) and in defining the pathogenetic type of pulmonary edema (hydrostatic v increased permeability). This hypothesis is based on theoretical concepts regarding the mechanisms responsible for the relaxation times and the state of water in biologic systems. According to these concepts, the relaxation times T_1 and T_2 in biologic tissues are affected not only by water content, but also, among other factors, by the interactions between

water and macromolecules.[14,42–44] According to simple two-state models,[14,42–44] biologic tissues contain two fractions of water: free water and water bound to macromolecules. If the model also assumes a fast exchange between the free-water compartment and the bound-water compartment, the spin-lattice relaxation rate ($1/T_1$) is the weighted average of the relaxation rates of the two compartments:

$$1/T_1 = (1/T_1)_b F_b + (1/T_1)_f(1-F_b)$$

where $(1/T_1)_b$ and $(1/T_1)_f$ are the relaxation rates for the bound- and free-water compartments, respectively, and F_b is the bound-water fraction. According to this equation, T_1 is dependent on the ratio of free to bound water. Quantitatively, the influence of the free- to bound-water ratio on T_1 is enhanced by the value of $(1/T_1)_b$, which, in biologic tissues, is much greater than that of $(1/T_1)_f$. The dependence of T_1 on water-macromolecule interactions is reflected by the experimental finding that $1/T_1$ correlates closely with protein concentration in water solutions[14,42,44–47]; this dependence probably represents an important cause of T_1 variation among different biologic tissues.[44]

Experiments on mouse lungs in which either or both of the 90-degree and 180-degree pulses used in the spin-echo sequence can be either soft (ie, long compared to T_2 and thus frequency-selective) or hard (ie, short compared to T_2 and thus nonselective) have been able to resolve the fraction of water bound to macromolecules ν the free water.[48] More recently, a theoretical expression has been derived for the proposed mechanism that the spin-lattice relaxation arises from water-biopolymer cross-relaxation.[49] The expression states that, for this mechanism, $1/T_1$ should vary linearly with $\nu^{-1/2}$, where ν is the NMR frequency. Experimental measurements of $1/T_1$ as a function of ν in rat lungs have confirmed this prediction.[49] Recent pulsed-magnetic-field gradient NMR diffusion measurements of rat lung tissue have shown that the self-diffusion coefficient[14,42] is nearly an order of magnitude smaller than that of free water and is nonbrownian in character.[50] This experiment demonstrates that the motion of water in normal lungs is considerably more restricted than that of free water.

The above concepts are of particular interest with respect to the study of pulmonary edema. A fraction of interstitial lung water is associated with the macromolecules that constitute the matrix of the lung (collagen, elastin, proteoglycans, and fibronectin),[51–55] with cellular macromolecules, and with other molecules (including plasma proteins). This fraction corresponds to the bound-water fraction (F_b) in the above equation for $1/T_1$. In pulmonary edema, the accumulation of water in the interstitial spaces can be expected to cause an increase in the free-water fraction, which should increase the value of T_1 according to that equation. Since the bound-water fraction is proportional to protein concentration,[14,42,44] the equation also predicts that, for the same lung water content, T_1 should vary according to the pathogenetic type of pulmonary edema. In hydrostatic (high pressure) pulmonary edema, the protein concentration of the edema fluid is low because interstitial proteins are washed out by the increased lymph flow and are not replaced (microvascular permeability is normal).[56] In contrast, in increased permeability lung edema, the protein concentration of the edema fluid is normal or elevated because of the increased transcapillary protein leakage.[56] Therefore, the free- to bound-water ratio and the value of T_1 should be higher in hydrostatic than in increased permeability lung edema.

Podgorski and associates[41] tested these concepts by measuring the relaxation times of lung lymph obtained from chronically instrumented nonanesthetized sheep after the administration of *Escherichia coli* endotoxin (causing increased permeability edema) or the insertion of a left atrial balloon (causing hydrostatic edema). As predicted, they found that the lymph T_1 value was higher when pulmonary hydrostatic pressure was elevated than when capillary permeability was increased. However, Huber and Adams[24] found no difference between the lung T_1 values obtained from rabbit models of hydrostatic (by aortic balloon and saline infusion) and increased permeability (by oleic acid) pulmonary edema.

Other investigators have tested the hypothesis, based on the same principles, that T_1 measurements can differentiate pulmonary edema from other pathologic conditions. Huber and Adams[24] compared T_1 measurements obtained from rabbit models of lung hemorrhage (induced by endobronchial instillation of blood) and pulmonary edema (hydrostatic or increased permeability) and found no differences between these conditions. However, they observed the longest T_1 values only in the models of pulmonary edema. Similarly, in an NMR imaging study of patients with various types of air-space disease (eg, edema, pneumonia, or hemorrhage), Moore and coworkers[35] found a considerable overlap between edema and other pathologic conditions; again, the longest T_1 was observed in a patient with acute cardiogenic pulmonary edema. Shioya and associates[28] found that, in rats exposed to high concentrations (80% to 100%) of oxygen, T_1 increased with water content during the acute phase of the injury but decreased more markedly than water content during the repair stage. As discussed by those authors,[28] the NMR response to high concentrations of oxygen can be explained on the basis of the corresponding structural changes. The initial increase in T_1 likely reflects an increase in the free-water fraction due to edema; the subsequent disproportionate decrease in T_1 may reflect an increased bound-water fraction due to structural changes associated with the repair stage of the injury (ie, proliferation of interstitial cells with an accumulation of new collagen and elastin).[57] An increased bound-water fraction due to an increased concentration of macromolecules may also partly account

for the decreased T_1 values observed by Vinitski and associates[58] in rat lungs with bleomycin-induced injury.

Since the spin-spin relaxation time T_2 is, like T_1, dependent on tissue type,[43,44] it too is a potentially useful complement to proton density data. Although some experimental evidence supports this prediction, the published data are not entirely consistent. T_2 has been found to differ between hydrostatic and increased permeability edema[23] and to be shorter in bleomycin-induced pulmonary fibrosis.[58] In the study mentioned above by Shioya and coworkers,[28] the exponential components of the lung T_2 decay obtained from rats exposed to high oxygen concentrations showed changes similar to those of T_1. However, other studies showed no significant differences in T_2 between pulmonary edema and other pathologic conditions or between hydrostatic and permeability lung edema.[24,35,41]

The above experimental results are not conclusive. On the whole, they suggest that relaxation time measurements can complement the proton density data, at least under certain experimental conditions. However, the practical value of this combined (T_1, T_2, and proton density) approach remains to be proved. An important limitation to consider is the overlap between relaxation times obtained in different pathologic conditions.

NMR PROPERTIES OF INFLATED LUNGS

It has been shown that the NMR free induction decay, as described earlier, is much shorter in inflated lungs than in collapsed lungs.[18] This extra signal loss, which can be reversed by a spin-echo sequence, is due to the presence of internal, tissue-induced magnetic field inhomogeneity produced by the alveolar air-tissue interface (because of the different magnetic susceptibilities of water and air). The internal magnetic field inhomogeneity, which has been explained using theoretical models and simple phantoms,[59] can also be detected with temporally symmetric and asymmetric NMR spin-echo radiofrequency sequences. Such sequences generate a pair of NMR images (symmetric and asymmetric) from which a difference image is obtained.[17,18] An important additional confirmation of this phenomenon has been provided by observations of a linear dependence of the reciprocal of the internal tissue-induced free induction decay time (T_2') on the external magnetic field B_0.[49] This dependence is to be expected from the fact that diamagnetic susceptibility differences between air and water should be proportional to B_0.

Since the difference image reflects the signal from water experiencing the air-tissue interface effect, the symmetric-asymmetric subtraction technique is of interest with respect to the assessment of lung edema. A potential application of the technique in this area could be the partitioning of lung water into a fraction close to and affected by the air-tissue interface (interstitial edema) and a fraction uninfluenced by the distant air-tissue interface (interstitial edema and alveolar flooding).

ADVANTAGES AND LIMITATIONS OF NMR ASSESSMENT OF PULMONARY EDEMA

NMR techniques appear to be particularly attractive because, unlike several other methods for measuring lung water, they are not invasive. Although the data acquisition time may vary depending on several factors (eg, the technique, the signal-to-noise ratio, the desired resolution, and the elimination of artifacts), NMR measurements are relatively rapid, the time needed for imaging being on the order of seconds to minutes. The application of fast imaging methods[60–65] could further reduce the image acquisition time; however, the use of fast imaging for lung water quantitation has not been tested. Recent studies of experimental models of lung injury in rats suggest that NMR measurements are at least as sensitive as the gravimetric technique to changes in lung water content.[31] The measurements are easily repeatable and allow the time course of lung injury to be defined.[28,31] An important advantage of NMR imaging is its ability to assess the spatial distribution of lung water, since the data employed for water quantitation are those used to construct the NMR image. The nonspatial $V_f \nu \rho H_2O$ distribution analysis[31] promises to complement the spatial approach.

The application of NMR techniques to the study of pulmonary edema also has significant limitations. Compared with other organs, the normal inflated lung generates a weak proton NMR signal because of its low water density. This limitation, which has led some investigators to question the role of NMR in the study of the lung,[66] is much less important in the edematous lung, in which water density and therefore the NMR signal are markedly increased. In addition, as discussed in detail elsewhere,[5] the measurement of the NMR signal from the lungs can be improved by using higher magnetic fields and a temporally symmetric gradient sequence and by other technical measures. In rats with oleic acid–induced pulmonary edema (and in normal controls), Schmidt and coworkers[22] increased the intensity of the NMR lung signal at short repetition times (0.5 seconds) by the administration of the paramagnetic agent gadolinium diethylenetriamine pentaacetic acid (Gd = DTPA), a substance that markedly reduces the relaxation times T_1 and T_2. These investigators suggested that Gd-DTPA might be used to decrease data acquisition time.

Another significant problem is the differentiation of pulmonary edema from other causes of increased proton density (eg, atelectasis or pneumonia). [A concomitant chest radiograph would usually solve this problem.—Ed.] A possible solution to this problem would be to characterize these various pathologic conditions by relaxation time measurements. How-

ever, the available data are not conclusive, especially because some studies have shown considerable overlap in the T_1 and T_2 values between different pathologic conditions.[24,35] It should also be noted that the differentiation between various causes of increased proton density may be more important in clinical applications of NMR to the assessment of pulmonary edema than in some specific experimental situations (when predictable models of lung injury are used and the predominant concern is quantitation, rather than characterization, of the injury). The recently described unique NMR behavior of the inflated lung should allow identification of even partially aerated lung tissue from nonaerated tissue.[18]

At their present stage of development, NMR techniques cannot discriminate between intravascular and extravascular lung water. This limitation, which represents a particular aspect of the general problem of tissue characterization discussed above, is important for the differentiation of pulmonary edema from vascular congestion. Skalina and coworkers[25] proposed differentiating intravascular from extravascular lung water on the basis of the different relaxation times of blood and edema fluid (which is assumed to be similar to plasma in protein content). Montgomery and associates[67] reported evidence suggesting that the paramagnetic agent Gd-DTPA, when administered by aerosolization, may selectively enhance the NMR signal from extravascular-extracellular lung water. They proposed that aerosolized Gd-DTPA could distinguish the extravascular-extracellular lung water compartment from the intravascular compartment, and therefore could be useful in the assessment of pulmonary edema. [This approach, while interesting, would appear to raise some clinical problems.—Ed.] In addition, since the exchange of sodium between intravascular and extravascular compartments is slower than that of water protons, the use of sodium imaging in combination with proton imaging and the administration of the intravascular superparamagnetic agent magnetite-dextran (to suppress the intravascular sodium signal) has been suggested as a possible means of assessing the distribution of lung water between the two compartments.[40] These and other potential solutions are still at a very preliminary stage of experimentation and need further testing, especially to assess the importance of possible limitations.[68] Although in principle the NMR techniques measure total lung water content, intravascular lung water is likely to be underestimated because the intensity of the NMR signal from flowing blood decreases at high flow velocities.[69–71] [This is a particularly important clinical problem since transit time diminishes with overhydration but increases markedly with cardiac failure.—Ed.]

The determination of absolute lung water content requires appropriate technical procedures (eg, adequate repetition times, correction of reduced NMR signal intensity due to the T_2 decay, use of a temporally symmetric gradient sequence, and minimization of motion artifacts) that may substantially increase the data acquisition time. In addition, simplified procedures for T_2 correction (from images obtained at two echo times) have been found to be satisfactory for excised rat lungs studied at a low level of inflation[33] but less so for intact living rats, possibly because the T_2 decay was not characterized by a single exponential.[31] For these reasons, most investigators have used uncorrected NMR signal intensity data as relative measures of lung water content; the good correlation observed between uncorrected NMR data and gravimetric lung water content in various models of experimental lung injury, as described above, indicates that uncorrected NMR measurements are adequate for the assessment of pulmonary edema. [It would be more accurate to say that uncorrected NMR measurements are adequate for the assessment of *lung water* since pulmonary edema is strictly extravascular water.—Ed.]

As discussed in detail elsewhere,[5] respiratory motion can affect lung water quantitation. The effect of respiratory motion depends on the NMR technique used (eg, the line-scan technique is less sensitive to motion than two-dimensional Fourier transform techniques) and can be reduced by respiratory gating or other methods.[5,72–78] However, experimental evidence suggests that conventional nongated NMR measurements adequately reflect relative lung water content changes in small mammals with pulmonary edema.[22,23,31]

The problems posed by the practical application of imaging and nonimaging techniques in basic research and clinical medicine have been discussed in detail elsewhere.[5] Lack of mobility of the NMR imagers is not a serious problem in NMR research or many areas of clinical medicine, but it does limit the clinical application of NMR imaging in critically ill patients. The effects of the magnetic field on monitoring instruments and supportive equipment (such as mechanical ventilators and infusion pump devices) as well as distortions in the magnetic field due to the presence of metallic objects are at least partly solvable; for instance, fluidic ventilators (which have no electronic components) or other types of ventilators can be used effectively in combination with NMR imaging.[79–82] Hedlund and associates[81] recently described a ventilator that is compatible with the NMR imaging system and that eliminates the effects of respiratory motion. The effect of the magnetic field on metallic implants requires special precautions for patients with cardiac pacemakers, surgical clips, prostheses, or other implants.[10,16,83,84]

CONCLUSION

In the past few years considerable progress has been made in the application of NMR imaging or nonimaging techniques to the assessment of pulmonary

edema. The NMR measurement of absolute water content is still at a preliminary stage because it requires special technical procedures that increase data acquisition time and poses problems not entirely solved. However, recent studies have demonstrated that conventional NMR techniques can adequately detect and quantify relative changes in water content in pulmonary edema. Therefore, these studies have established a new role for NMR in basic research as a reliable method for detecting and monitoring lung injury. Although they are far from conclusive, recent attempts to characterize pathologic abnormalities in the lung by relaxation time measurements are of interest because, if pursued systematically, they could ultimately lead to a more comprehensive NMR assessment of pulmonary edema (and of lung injury in general).

Applications of NMR techniques to the quantitation of lung water in humans have been sparse, and the value of such techniques in the assessment of clinical pulmonary edema is virtually unexplored. However, available experimental evidence is encouraging. Preliminary data show that NMR methods tested in animal research can be applied to humans. Therefore, NMR quantitation of relative lung water changes in clinical pulmonary edema should be feasible. The application of NMR imaging to the assessment of pulmonary edema in clinical medicine could substantially benefit from recently developed fast imaging techniques and from the suppression of artifacts due to respiratory motion. The potential of NMR imaging in the evaluation of the spatial distribution of lung water makes this technique particularly attractive for both basic research and clinical medicine.

As discussed above, some of the problems posed by the practical application of NMR techniques (eg, the effects of respiratory motion and incompatibilities between the imaging system and standard ventilators) have been at least partially solved. The solution of other problems (eg, discriminating between intravascular and extravascular lung water, distinguishing pulmonary edema from other causes of increased proton density, and standardizing methods for the measurement of absolute lung water content) is an important area for future research.

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