In the Name of God

SHIRAZ UNIVERSITY OF MEDICAL SCIENCES

SCHOOL OF DENTISTRY

THESIS

FOR DMD DEGREE

MAGNETIC RESONANCE IMAGING IN DENTISTRY

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FALL 1368 / 1989

No :

ارزیابی پایان نامه

پایان نامه شماره :　　　　　　　　　　تحت عنوان : M.RI

تهیه شده توسط :　　　　　　　　　　در کمیته بررسی پایان نامه مطرح و

با درجه / نمره :　　　　　　　　　　به تصویب رسید .

استاد راهنما : دکتر　　　　　　سمت :

امضاء

اعضاء کمیته بررسی :

۱-

۲-

۳-

۴-

ACKNOWLEDGEMENT

I would like to express my deep appreciation to my teacher Dr, E. Mozaffari oral radiologist and assitant professor of oral radio - logy department of school of dentistry , Shiraz University who has offered valuable assistance & criticism in the preparation of this thesis .

Also I would like to thank Mrs. Hosseinpour for typing this manuscript .

To my parents

who constantly encouraged me

to go forward

And:

To my wife

Mojgan

CONTENT

INTRODUCTION

Nuclear Magnetic Resonance (NMR),[43] a new diagnostic imaging modality , is receiving a great deal of attention and is generating the most excitement in the medical and dental community since the advent of X-ray computed tomography . The reason for this excitment is the capability of NMR to generate high resolution , diagnostic quality medical images at any angle and projection of the human body without ionizing radiation .

In addition , NMR provides in vivo data concerning human biochemistry and pathophysiology based upon subatomic physical principles and interaction . This , in itself , may revolution - ize medical diagnostic imaging .

The physical basis for NMR imaging involves the interaction of the nuclei of a selected atom (for example , hydrogen), which may be part of many molecules in many human cells , with an external magnetic field and with an external oscillating (radiofrequency) electromagnetic field that is changing as a function of time at a particular frequencey .

The idea of resonance resulted from observation in the 1940's that energy is absorbed and subsequently released by the selected nuclei at particular frequencies following irradiation with radiofrequency (R F) electromagnetic energy .

Several biologically interesting atoms have nuclei with magnetic properties that may be studies using NMR techniques . These isotopes or nuclides [46] (e.g., hydrogen , carbon - 13 , flourine - 19 , sodium 23 , and phosphorous - 31) are unique in that their nuclei contain an odd number of nucleons (protons and neutrons) . They therefore possess properties called angular momentum and spin , which can be measured for NMR spectroscopy and NMR imaging .

Most efforts to date have concentrated on NMR imaging of the proton distribution because of its natural abundance and its relatively strong signal compared to other nuclei .

Creation of NMR images involves use of a large resistive or superconducting magnet . Attached to this are magnets of lesser strenght and an energy source . The selection of the plane , planes , or volume of interest is controlled through a computer similar to the type used in X-ray computed tomography , and the image or data generated is displayed on the comptuer terminal . The opening in the magnet for the patient or sample closely resembles the gantry in a C T scanner . To the patient experience will be similar to that of having a C T scan .

Several recent articles have interpreted the physical principles [5,32] and instrumentation used in NMR imaging .

Recent reports describe initial clinical results at several centers . It appears that NMR imaging is able to diagnose, many, if not all , of the anatomic changes seen with X-ray computed tomography . In addition , due to the inherent contrast[7] resolution capability based on bassic NMR parameters including nuclear density (P) and relaxation times (T_1 and T_2) , several kinds of lesions have been demonstrated by NMR which cannot be seen using X-ray C T .

Further , the ability to observe metabolism [17] in vivo using NMR techniques can only be approached with positron emission tomography . Numerous clinical cases have been reported correlating CT and NMR in neoplastic , inflamatory , embolic , and traumatic lesions of the brain , face , thyroid , lungs , heart , liver , pancreas , kidney , pelvis , TMJ and extremities .

One of the most exciting areas of NMR development is gated cardiac imaging in medicine , and TMJ imaging in dentistry which will be discuss later .

The impact of NMR imaging and diagnostic techniques in clinical medicine or dentistry is likely to be profound . Clinical efficacy studies , will define the role of NMR techniques in comparison with various other imaging and diagnostic modalities over the next years .[5]

It is important that interdisciplinary teams of physicians, physicists , and engineers work closely and effectively as NMR imaging techniques are developed , evaluated , and place " on line " in the health care system .

The main goal of this theses is to discuss about NMR and then introduce its application in dentistry and compare it with other imaging techniques .

In dentistry , MRI is now well stablished as a valuable imaging modality . Recent studies reporting tempromandibular joint (TMJ) examination by magnetic resonance imaging (MRI), in many ways . And also its use in diagnosis of malignant head and neck tumors is very important .[7]

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REVIEW OF LITERATURE

Although NMR has come to the fore as a modality of medical imaging rather recently , the fundamental phenomenon of nuclear magnetic resonance is much older . The basic discovery of nuclear magnetic resonance was made in the United States by two group working independently , one led by Bloch [19] and the other by Purcell[19], their results were published almost simultanously in 1946 . For this discovery Bloch and Purcell were jointly awarded the Nobel Prize for physics in 1952 .

Since that time NMR has had a tremendous impact in physics[43], chemistry , and other discipline , and has become a standard method of spectroscopic investigation of matter in all its forms. NMR spectrometers are now part of the regular instrumentation of well - equipped chemistry and physics laboratories , where they provide indispensable technique for the structural , analytical , and dynamic ivestigation of liquids and solids . This may be described as the era of conventional NMR spectroscopy .

In conventional NMR one usually works with a small specimen , typically 1 ml or less , of pure homogenous liquid or solid , and place this specimen , in the most uniform magnetic field available , perhaps uniform to 1 part in 10^9 over the specimen . In NMR imaging we have just the opposite circumstance : the object of interest is not homogenous , it is heterogenous , it may not be small , and we place it in a deliberately non uniform magnetic field .

Felix Bloch [46] performed the first biologic NMR experiment in 1946 , when he placed his finger in the probe coil of his first NMR spectrometer and obtained a strong proton NMR signal.

It was , however , an integrated signal from the protons in the blood , tissue , fat , bone marrow , and other components of his finger and provided no spatial information concerning the disposition of those components.

NMR Scaning [43] for medical diagnosis was first reported by Damadian in 1971 followed by others . The rapid development of this idea from its first conception in 1969 to its practical realization in the first body scanning machine , accomplished in 1977 , reflects its medical promise . Since the first human[43] scan , other groups have also successfully accomplished human images .

The 1971 study , was also the source of a secound observation that has proved particularly valuable to groups making NMR images . Out of the need to stablish , the normal T_1 values to compare with the T_1 values of cancer tissur , is different . The result stablished that not only could the NMR signal distinguish between the normal tissues, but also each normal tissue had its own characteristic T_1 value .

The T_1 value , for example , of two soft tissues such as kidney and small intestine whose X-ray transmittances differ by less than 1 percent and are consequently difficult to distinguish radiologically without contrast agents , differed by nearly 100% percent in T_1 .

The use of T_1 has produced pictures with far more tissue contrast than ever before imagined for the techniques on non-invasive imaging , the most notable of which are the current T_1 images of the brain that clearly distinguish gray and white matter .

Among[46] the point scanning methods , Damadian's " Field Focusing NMR " (FONAR) technique was used to obtain whole-body NMR inage in 1977 and is currently being evaluated clinically .[42]

The first images from a live human subject were produced by Mansfield and Maudsley in 1976 using a Line - Scanning (class of NMR imaging methods in which spin - density distribution is interrogated one line at a time . Line is scanned sequentially through the sample to obtain the complete image) technique . Cross - sectional images were obtained through the mid - phalanx of the finger , showing the best soft tissue resolution by NMR thus far .

Subsequently the method was used to obtain whole - body images and localized a tumor in a postoperative mastectomy specimen . This technique has also been used to obtain images of the normal human head by Holland et al.

The first medical image produced by magnetic resonance was reported by Lauterbar in 1973 .[11]

By 1985 , there were approximately 200 MRI units operating throughhout the world with 70% of the total in United States.

The first reported use of MRI for temporo-mandibular joint (TMJ) evaluation was by Helms and Coworkers in 1984[11] . Image quality at that time was limited by low resolution and thick sections . The advent of image - intensifying surface [3] coils was allowed diagnostic imaging of small structures such as the TMJ .

Basic NMR principles and applications have been reviewed by Scherzinger and Hardee and Moon and Coworkers[38] . In 1987 , Katzberg[26] and Coworkers Harms[20] and Coworkers , and Roberts and associates described refinements in techniques and findings in disk pathology .

Katzberg and associtesd[26] compared normal joints in 5 subjects with abnormal joints in 37 patients in 1986 .

And recently the role of magnetic resonance imaging in the diagnosis and management of head & neck tumors , particularly ameloblastoma,[21] is very important , and also we know that imaging of maxillofacial anatomy is difficult , because of the compact arrangement of anatomic structures with different com - position , but with the role of MRI it is very easy to distinguish these structures .

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PHYSICS OF MRI[5]

Some [46] NMR phenomena can be explained only by quantum mechanics , but those relevant to the present discussion can be understood more easily through the principles of classical mechanics and magnetism .

MRI [32] studies differ from radiographic studies , which rely on object density to absorb transmitted x-rays . MRI relies on the phenomenon of NMR to produce a signal that can be used to construct an image .

The NMR phenomenon occurs because of several factors . Objects that are charged and move induce magnetic fields . Therefore , atoms having an uneven number of protons and / or neutrons in their nuclei (nucleides) have a spin that produces magnetic dipoles . Since these dipoles can be affected by external magnetic forces , a strong external magnetic field aligns these nuclei if their environment allows mobility .(Fig. 1)

Another NMR phenomenon is precession of nuclei around the axis of the external magnetic field . This motion is similar to that of a top that precessess around an imaginary axis as it spins (Fig. 2). The frequency of this precession in termed the *Larmor frequency* , and is dependent on the nuclide and the strenght of the external magnetic field . For example , this frequency is a constant 63 . 86 megahertz (MHz) for the proton (H^+) in a 1.5 Tesla field . The resonance frequency is directy proportional to the strenght of the static field according to the formula :[43]

$$Wo = \gamma \, Ho$$

$$Vo = \frac{\gamma}{2\pi} Ho$$

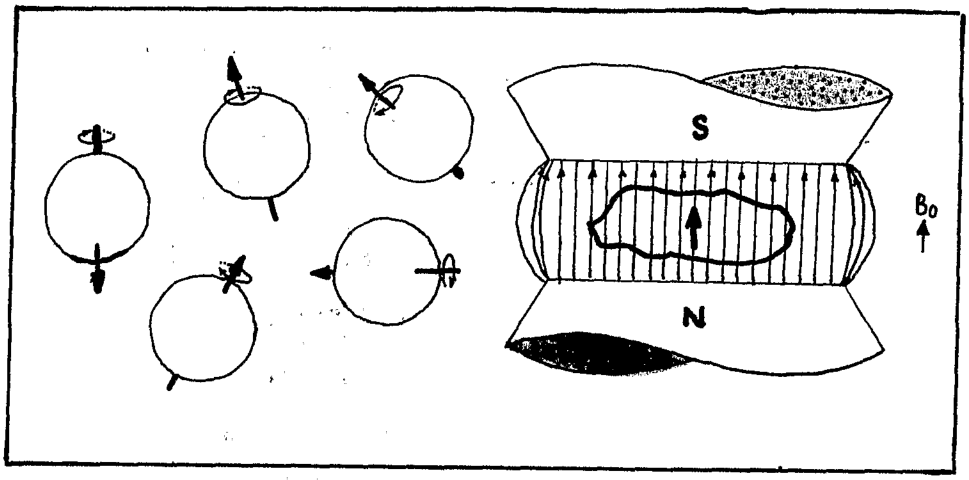
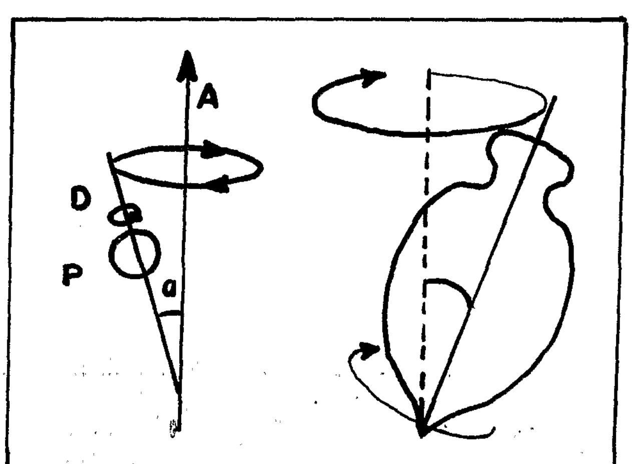


Fig. 1a:In the absence of any externally applied magnetic field, individual nuclear magnetic dipoles within a sample are randomly oriented . b: When a uniform, static, magnetic field (B_0) is applied, a preponderance of NMR-sensitive nuclei will aligh themselves with the lines of magnetic induction in such a way that a net magnetic moment is generated within a sample. (N = north , S = south).

Fig. 2: Precessional movement of a proton (P) spinning on its axis (D) around axis of main magnetic field (A) is similar to motion a spinning top makes as it loses its spin. System is in its lowest energy state when angle (a) is closest to zero.



Where W_o = Larmor frequency (radian per sec)

V_o = Larmor frequency (H Z)

γ = The magneticogyric ratio

and H_o = Strenght in Tesla of the applied field

A third NMR phenomenon is the ability of nuclei that meet the aforementioned criteria to absorb energy from radio - fre - quency (RF) waves of the Larmor frequency . This absorbed energy enlarges the angle of precession of the nuclei (Fig. 3). When thus excited , the nuclei initially precess in phase with one another (Fig. 4).[32] The following excitation , the nuclei relax to a lower energy state by decreasing their angle of precession and emitting the absorbed energy as an RF wave at Larmor frequency . It is this signal that makes an MRI possible .

During clinical MRI studies , the subject is placed in a uniform magnetic field . Secondary coil in planes at right angles to the main magnetic field provide a gradient such that each volume (called voxel) in space within the field has a slightly different magnetic field associated with it , than the protons in any other voxel . This spatially encodes the data , allowing computation of images .

Protons in the area of interest are energized by RF pulse at the appropriate Larmor frequencies . The signal generated by the relaxation of the protons is affected by the following :

1. *Proton abundance* (also referred to as rho or proton density). This terms refers to the number of protons in the voxel that contribute to the signal .

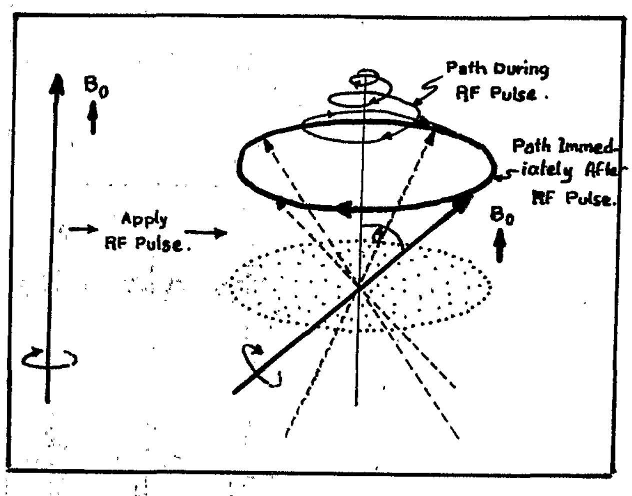


Fig. 3: Upon application of a radiofrequency (RF) pulse, the net magnetic moment is perturbed from its equilibrium position, and because of its properties of spin, begins to precess about the static field direction. The angle between the axis and the magnetization vector continues to increase as long as the pulse remains on. When it is turned off, the vector precesses freely at the final angle, θ, and its rotation describes the wall of the cone . The component of magnetization which rotates in the X,y plane (shaded area) generates the nuclear signal .

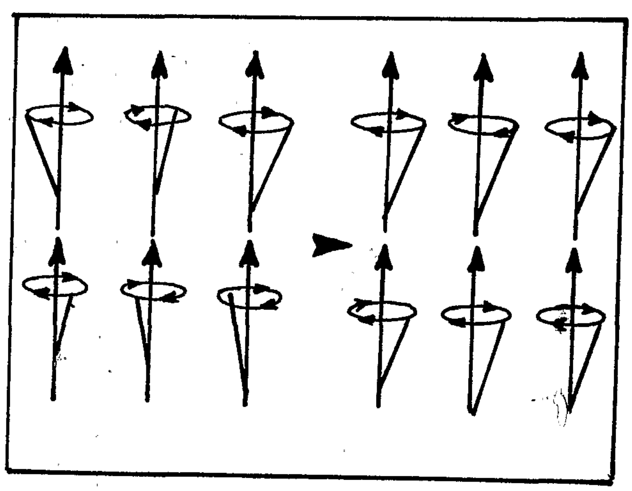


Fig. 4: Protons precessing out of phase (left became phased right) immediately after excitation from a radio wave of proper frequency (Larmor frequency).

2. *Motion* (of which blood flow is physiologic compone - nt) . This results from the change in location of the protons during the time the study is in progress .

3. *Longitudinal relaxation time* (also reffered to as T_1 or spin - latice relaxation time) . This refers to the lenght of time it takes for the angle of precession to relax to mini - mal energy state .

4. *Transverse relaxation time* (also reffered to as T_2 or spin - spin relaxation time) . This term reffers to the lenght of time it takes the excited proton precessing in phase to be - come dephased . T_2 is dependent on the intrinsic fields within the nuclear environment .

The [46] factors which determine T_1 and T_2 are numerous , but particular ones may be of interest in imaging biological systems . T_1 and T_2 are most sensitive to the degree of molecular motion . In solids and at low temperatures , there is little molecular motion and T_1 may be many seconds while T_2 is only microseconds . However , in liquids and at higher temperatures, T_1 and T_2 are almost equal , both being about 2 seconds for pure water . (In fact , T_2 can never be longer than T_1 and often substantially shorter) . In NMR imaging , only the signal from " liquid - like " regions is observed , rigidly bound nuclei give essentially zero signal .

Variation in T_1 proton relaxation time among different tissues are often related to free water content . Interestingly, malignant tissues appear to have higher T_1's than do corresponding normal tissues , which may be just a result of the larger amount of water present . Elevated T_1's have been reported in a variety of other human diseases , and have also been related to growth rate .

The [4] selection of an appropriate RF pulse sequence energizing the protons determines the weight each of the above factors contributes to the total signal . This allows tailoring of the examination for specific tissue characteristics . For example , a T_2 weighted image can often indicate areas of inflammatory or degenerative changes within a tissue . MRI can often demonstrate the early onset of these changes .

Three different pulse sequences are commonly used for clinical MRI imaging . The *partial saturation* sequence is the most rapid of the different pulse sequences currently in use . It consist of a series of 90 - degree RF pulses with an equally spaced repetition time (TR) between each pulse . More pulses improve the signal - to - noise ratio of the image . However , increasing the number of pulses also increase the lenght of time required for the procedure .

Partial saturation sequence imaging , which uses a TR greater than the longest T_1 of the tissues being imaged , will result in a *Proton abundance - weighted* image . Lowering the TR will result in more T_1 weighted images .

The *inversion - recovery* sequence is similar to partial saturation except that a series of paired pulses is used instead of single pulses . The first of the pair is a 180 - degree RF pulse that aligns the protons opposite the magnetic field. The second pulse occurs after a specific interpulse interval (T int) and consists of a 90 - degree RF pulse . TR in this instance refers to the repetition time between 180 - degree RF pulses . Changing the TR determines whether the image is a proton abundant or T_1 weighted image . By altering the T int the relative contrast between tissues of differing T_1 s can be enhanced .

In the *spin - echo* sequence , a 90 - degree pulse is followed by a 180 - degree pulse . This gives an image composed of both T_1 and T_2 elements . If the time interval between the 90 - degree pulse and 180 - degree pulse is termed T int and echo will be produced at time 2 T int , also know as *echo delay* (TE). By altering TE and TR (the time between 90 - degree pulses) the images can be weighted toward either T_1 or T_2 . (Increasing TR leads to a more T_2 weighted image).

Multiple echoes can be obtained without increasing the data acquisition time . Earlier echoes will be more T_1 weighted , whereas later echoes will contrast tissues within long T_2 relaxation values .

As relaxation progresses the signal strenght decreases with each successive echo . Thus the signal - to - noise ratio decreases with each successive echo .

GENERATION OF STATIC MAGNETIC FIELDS:[46]

The signal - to - noise ratio of an NMR image can be increased by increasing the strenght of the applied magnetic field. However , there are limitations to the use of this relationship in clinical scaning , since higher magnetic fields require higher RF's and the attenuation of signals by tissue is greater at higher frequencies .

The static magnetic field strenght required for imaging , therefore , is relatively low by NMR standards .

For the biologically interesting nuclei (which have lower values of the gyromagnetic ratio) , higher magnetic fields are required to obtain data at constant frequency .

INTRAVASCULAR CONTRAST AGENTS SUITABLE FOR MRI:[50]

Despite the high tissue contrast intrinsic in magnetic resonance imaging (MR) , there is a need for intravascular contrast media to demonstrate differences in tissue function and perfusion : for example , current pulse sequences do not allow consistant differentiation of cerebral edema from neoplastic disease . Many experiments had conducted in vitro and in vivo to evaluate the potential role of the paramagnetic contrast agents *chromium (Cr) EDTA* and *gadolinium (Gd) DTPA* in MR .

In these experiments , sodium salt of *Cr - EDTA* and *dimethyl glucamine salt of Gd - DTPA* were employed . A 50 mg / ml solution of Cr - EDTA was prepared from the dry powder for intravenous (IV) injections , the concentration of free chromium at a physiological PH was less than 10^{-10} M due to the K_{sp} (10^{-30}) for $Cr(OH)_3$.

After evaluating both agents , in vitro and in vivo studies shows that , MR signal intensity depends on proton density , T_1 , T_2 , and flow , each of which may be manipulated to improve tissue contrast .

However , the iodinated contrast agents used in conventional radiology do not effectively influence any of these parame-