Wofford College

Physics and Medical Application of Magnetic Resonance Imaging

Ivan Gu

Medical Physics

Dr. Salley

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Abstract

The invention of magnetic resonance image (MRI) utilizing Nuclear Magnetic Resonance (NMR) brought a tremendous influence in both the medical and physics community. Researchers first studied molecules ex vivo by taking samples and analyzed characteristics using NMR spectroscopy. They later applied fundamental NMR concepts such as nuclear spin, magnetization, and relaxation time to design machines that can non-invasively diagnose and treat patients with accuracy and efficiency. Currently, there are many MRI machines around the globe, making this medical procedure available to the majority of the population. While MRI can image many parts of the body, it is mainly focused on inflammation, neuropsychology, oncology, and cardiology. This is to detect infections within the brain, potential phyllodes, and cardiovascular muscle tears, respectively. Although there are safety concerns when the patient is not screened before the procedure properly, technology advancements have decreased the risk of injuries in patients and are serving to benefit society.

About 600 years ago, infectious diseases were the leading cause of death in Europe and America. At that time, the only available treatments included bloodletting, calomel, opium, etc. Fast forward 550 years, with the invention of magnetic resonance imaging (MRI), physicians can non-invasively look into interested parts of the patient's body and diagnose properly. The invention of MRI influenced the medical field significantly. The common problem of its ancestor, Computed Tomography, produces damaging ionization radiation to the patient. MRI is particularly useful and effective in imaging body tissues, spinal cords, and detecting tumors. The fundamental basis of this imaging technique is to manipulate the hydrogen nucleus inside the patients by introducing them to strong magnetic fields and form images using computations, knowing how body tissues react with such field. This paper addresses the background of MRI and its impact on society with focuses on the modus operandi of physics and its application in the medical field. Readers interested in biology and physics should continue reading as this paper explains MRI by combining these concepts yet refrains from being immensely technical.

An understanding of nuclear magnetic imaging (NMR) is required before the discussion of MRI. This phenomenon explains the interactions between the magnetic moments of the nucleus and magnetic fields. One of its properties, the nuclear spin, is a form of angular momentum possessed by these nuclei.[1] Atoms with an even number of protons and neutrons do not have nuclear spins, thus they will not be discussed in this paper. Atoms like hydrogen have an odd number of protons and neutrons, meaning they will rotate and have an orientation in an external magnetic field, providing useful information to scientists. The hydrogen atom is most commonly used in MRI because the human body is approximately 75% water, a molecule that

[1] Mlynárik, Vladimír. "Introduction to Nuclear Magnetic Resonance." Analytical Biochemistry, vol. 529, 2017

has two hydrogens. Hydrogen also exists in body fat, which makes up another 15% of the body.[2] Although other chemical compounds in the body contain hydrogens, MRI mostly focuses on the hydrogen nucleus in water and fat instead of those in protein, amino acids, or other macromolecules.

During an NMR, an object is first placed in a strong static magnetic field to align its nucleus of interest parallel to that field. When an orientation occurs, the magnetization of hydrogen precesses[3] with the direction of B_0 and has an angular frequency (figure 1), known as the Larmor frequency. Then the B_1 field is switched on for milliseconds, causing M to be tilted towards the two axes (figure 2). This is known as radio frequency (RF) pulses. Once these pulses are sent to the nucleus and have a specific amount of energy and frequency, its magnetic dipoles react and absorb and emit RF waves. Immediately following the pulse, resonance of the nuclei occurs and magnetization decays.

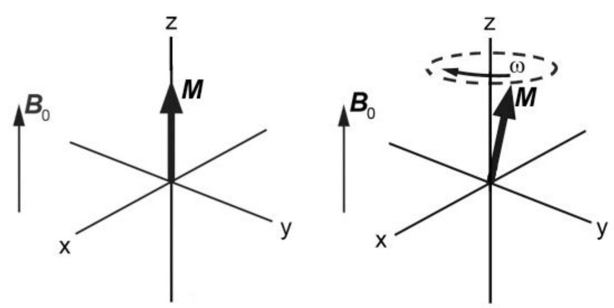

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Figure 1. A)Magnetization M aligns with the main static magnetic field B_0. B)Magnetization M precesses along the direction of B_0

[2] "Body Fat Percentage." *Wikipedia*, Wikimedia Foundation, 21 Nov. 2019, https://en.wikipedia.org/wiki/Body_fat_percentage.
[3] Change in orientation

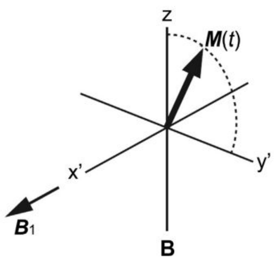

Figure 2. Magnetization M is tilted toward x′y′ plane by RF pulses.[4]

Magnetization is defined as the net magnetic dipole in a region containing many microscopic dipoles.[5] It is a vector of the sum of the individual magnetic moments. When in equilibrium, the magnetization vector points in the direction of the static field. Once an RF pulse hits, the nuclei will have magnetic moments which are then characterized by time in two components, longitudinally and transversely. The time for the magnetization to decay back to equilibrium is called relaxation time. Different matters will have different times to reach equilibrium, allowing scientists to analyze those properties and determine the probable matters using T1 and T2. T1 is defined as longitudinal relaxation time. It measures how long does it take for nucleus to realign with the main magnetic source (figure 1A). As the nucleus resonates back to equilibrium, the transverse component of relaxation time, T2, decreases. Typically, the longitudinal component increases while transverse component decrease. That is, more components become parallel to the main source and less of that continues to be perpendicular to the applied magnetic field (figure 3).

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[4] Mlynárik, Vladimír. "Introduction to Nuclear Magnetic Resonance." Analytical Biochemistry, vol. 529, 2017

[5] Kane, Suzanne Amador. Gelman Boris. Introduction to Physics in Modern Medicine. CRC Press, 2009.

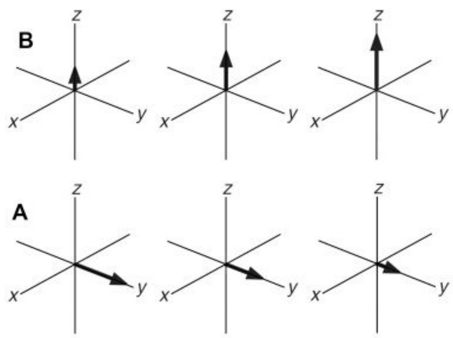
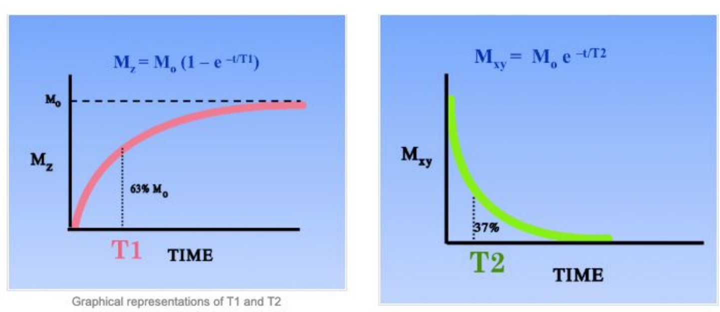


Figure 3. A)Transverse magnetization decreases with time constant T_2. B)Longitudinal magnetization resonates back to equilibrium with time constant T_1.[6]

The relationship between relaxation time constants and magnetization is characterized by Felix Bloch, known as the Bloch Equations. The magnetization that points parallel to the main field, conventionally in the z-direction, is related to T1, whereas the magnetization in the x'y' plane—orthogonal to the main field—is related to T2. The two time constants have distinct effect on the magnetization (figure 4). M_z increases along with independent variable—time—non-linearly. On the other hand, M_{xy} has an inverse relation with its independent variable.



A B

Figure 4. A)T1 represents the time it takes for M_z to increase to 63% of M_0. B)T2 represents the time it takes for M_{xy} to decrease to 37% of M_0.[7]

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[6] Mlynárik, Vladimír. "Introduction to Nuclear Magnetic Resonance." Analytical Biochemistry, vol. 529, 2017

[7] Bloch, Felix. *Nuclear Induction*. Phys Rev, 1946.

Since the factor of T1 and T2 appear to be complementary measurements of each other, it is surprising to see that the two times are not equal. This can be explained with variations around the nucleus. In the beginning, all the nuclei are pointing in the same direction longitudinally and transverse. But after a certain amount of time, even though the longitudinal direction did not change, the transverse component became disoriented. Without a consistent orientation, the free induction signal detected by radio receivers weakens and eventually loses that magnetization (figure 5).

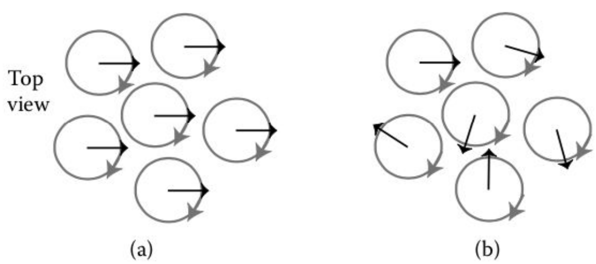

Figure 5. A)Orientation of the group of nucleus immediately after a pulse. B)After T_2, transverse component are oriented at random, thus losing magnetization.[8]

In terms of medical application, tumors have significantly different relaxation times than that of water—the main component of body tissues. Raymond Damadian, using NMR spectroscopy to study biological samples (figure 6), reported that some animal tumors have remarkably long photon relaxation time.[9]

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[8] Kane, Suzanne Amador. Gelman Boris. Introduction to Physics in Modern Medicine. CRC Press, 2009.
[9] American Chemical Society National Historic Chemical Landmarks, NMR and MRI: Applications in Chemistry and Medicine

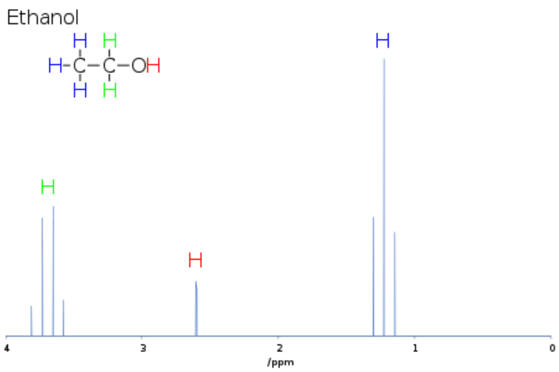
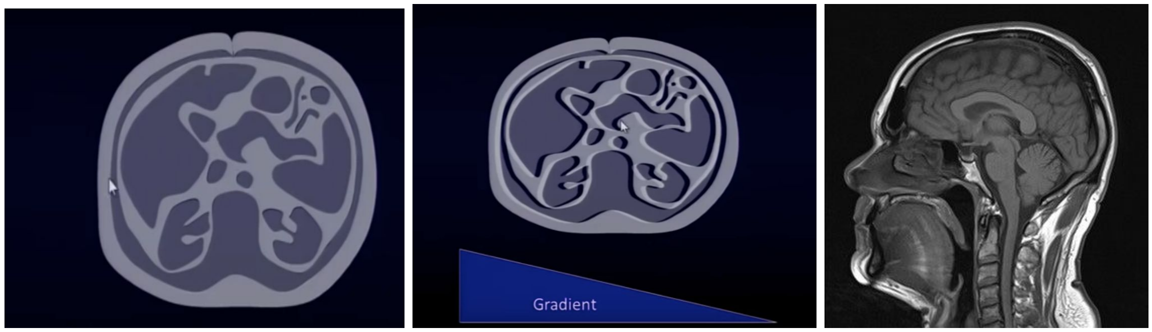


Figure 6. An example of Damaian's study of NMR spectrum, with the peaks caused by effects on the neighboring hydrogen atoms.[10]

Although impressed by this technique, Paul Lauterbur believed that ex vivo analysis of body tissues defeats the purpose of NMR. Lauterbur claimed that optical microscopy already provides rich information about tissue specimens, measuring their relaxation time may not give much additional information.[11] Prior to Lauterbur, all NMR equipments passed shim currents through thin coils of wire to manipulate gradients. To produce sharp NMR signals, those machines are programmed to eliminate field gradients—variation of the magnetic field strength in different positions. Although unique chemistry can be analyzed, spatial information between protons is lost. Instead of holding the magnetic field constant, Lauterbur used "sets of linear gradients oriented in different directions" to produce a multidimensional image from NMR signals of water and fat. The precession of hydrogen in water is faster than that of fat because it is not shielded by the electron cloud around the oxygen. By applying gradient, the image of water is pulled towards the stronger magnetic field (figure 7).

[10] "Nuclear Magnetic Resonance Spectroscopy." *Wikipedia*, Wikimedia Foundation, 14 Nov. 2019, https://en.wikipedia.org/wiki/Nuclear_magnetic_resonance_spectroscopy

[11] American Chemical Society National Historic Chemical Landmarks, NMR and MRI: Applications in Chemistry and Medicine



A B C

Figure 7. A)Superimposition of water and fat without gradient. B)The water image is being pulled left due to stronger magnetic field to reveal spatial and in depth information.[12] *C)Modern MRI scan of the brain, adopted from Lauterbur's model of using field gradient.*[13]

Physics, like many sciences, is never merely theoretical. MRI machines are one of the most common non-invasive imaging devices used across the world. Currently, there are over 50,000 of those machines in hospitals and medical facilities in the world, with an annual sale of 5000 machines.[14] Those machines are used to study and diagnose in numerous fields. This paper will focus on the diagnostics of infections, cancer, and cardiovascular muscle tears.

When children trip on the driveway while playing, their skin shows red burning marks. This is their immune system protecting and fighting off foreign invaders such as bacteria and virus. This is also a signal for the parents to put antibiotics on the wound to prevent further infection. When an infection inside the body exists, however, regardless of anyone's medical experience, they could not see or determine the severity of such conditions without taking a sample. While taking samples of soft tissues is possible, some parts of the body are designed not

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[12] Easy Radiology. "Physics Introduction to MRI." *YouTube*, YouTube, 23 Mar. 2018, https://www.youtube.com/watch?v=tcGG5njW890.
[13] "MRI." *NHS Choices*, NHS, https://www.plymouthhospitals.nhs.uk/imaging-mri.
[14] *How Many MRI Machines Are There?* https://www.magnetic-resonance.org/ch/21-01.html.

to be examined ex vivo such as brain infections. Those tissues cannot be sampled without damaging nerves. The "parents' eye" in this case is the Ga-DOTATATE PET/MRI[15]. As in its namesake, amino acid peptide Ga-DOTATATE can bond with gallium-68 and lutetium-177 to form radiopharmaceuticals.[16] Using this penetrating vision, one can see the illuminated region indicating a necrotizing granulomatous inflammation in the left temporal region (figure 8). Details of PET scan will not be addressed but fundamentally, a colorful image is produced by collecting photons from the annihilation of electrons inside the patient's body and positrons inside the injected tracers. PET highlights the abnormalities whereas MRI produces detailed body structure images. With the two combined, routine PET/MRI scans for patients can show physicans the progression or migration of the granulomas, helping them to determine the effectiveness of treatments. Because it is routinely used, patients do not need to make two separate appointments for PET and MRI. In addition, this combinational scan exposes less radiation to patients than that of PET/CT scans.

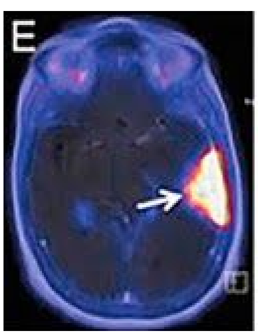

Figure 8. PET/MRI scan of a brain infection. The illuminated region are photons detected from annihilation of positrons and electrons.[17]

[15] Sollini, Martina, et al. "PET/MRI in Infection and Inflammation." Seminars in Nuclear Medicine, vol. 48, no. 3, 2018

[16] "DOTA-TATE." *Wikipedia*, Wikimedia Foundation, 23 Aug. 2019, https://en.wikipedia.org/wiki/DOTA-TATE.

[17] Sollini, Martina, et al. "PET/MRI in Infection and Inflammation." Seminars in Nuclear Medicine, vol. 48, no. 3, 2018.

After a few years of playing in the backyard or driveway, children enter puberty when their body characteristics start to develop. In Khouli and Louie's case study of enlarged mass in the breast of a 25 year old caucasian women, MRI along with other imaging techniques were used to conclude the benignity of such mass. Physicians first hypothesized the cause to be only hormone changes because of the patient's age, and given to only observe and no further treatments. Later diagnoses, using T1 and T2 axial MRI, speculate the mass to be either a giant fibroadenoma or phyllodes tumor. Fibroadenoma are benign tumors within breast areas. Usually a small lump, but in unusual situations it can show rapid growth, thus develops to a giant fibroadenoma. The most common occurrence appear to population under the age of 30. Phyllodes tumors exists in the same region. But most occurences appear in groups over 35. Both tumors are well defining shaped and freely mobile. Giant fibroadenoma are benign, whereas phyllodes can be both benign and malignant. Using Dynamic Contrast Enhanced Magnetic Resonance Imaging (DCE-MRI), where contrasts are injected inside the patient to reflect blood flows within organs, physicians constructed an enhancement pattern graph against time. Such graph is known as the kinetic curve. In this case, the right breast kinetic curve revealed a persistent pattern, suggesting its benignity. In addition, a pharmaco-kinetic color map reveals the permeability and K_{ep} value of the right breast (figure 9). Pharmacokinetics is the study of the body's response to certain drugs. The color map measures the body's response to the contrast agents used in DCE-MRI. Kep is adopted from Tofts model of DCE-MRI. This value is related to K^{trans} and V_e, characterizing the diffusive transport across the capillary endothelium.[18] In other

[18]Tofts, Paul S. "T1-Weighted DCE Imaging Concepts: Modelling, Acquisition and Analysis." MAGNETOM Flash, Brighton and Sussex Medical School, Mar. 2010, http://www.paul-tofts-phd.org.uk/DCE-MRI_siemens.pdf.

words, K^{trans} measures how fast a contrast used in DCE-MRI moves across a single layer of the cell. Blue and green indicates a low K^{trans} value, which is directly proportional to K_{ep} value. Lower K_{ep} value means the probability of a malignant tumor is lower. While Khouli and Louie cannot conclude whether this enlarged mass is either a giant fibroadenoma or phyllodes tumor, the contrast post map using data from DCE-MRI anecdoted a benign behavior of this enlarged mass.

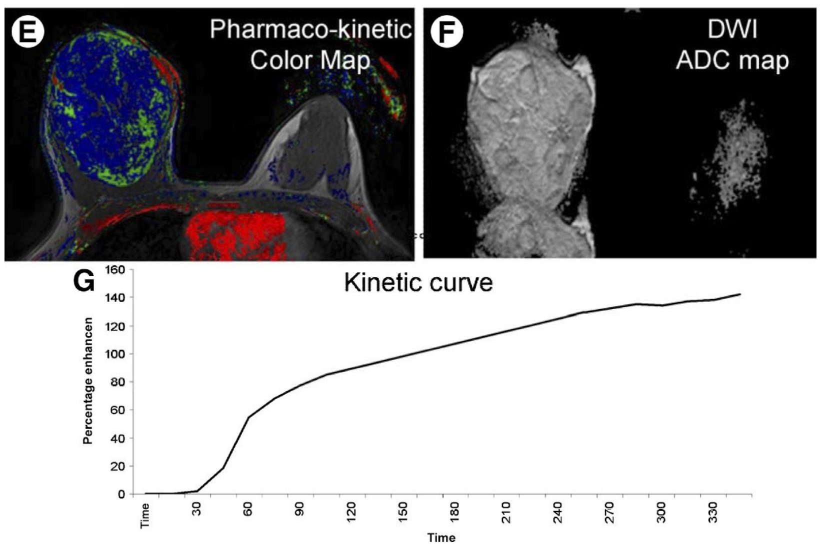

Figure 9. Blue and green reflection of the color map indicates a low permeability and Kep value on the right breast. Kinetic curve is the dependent variable percentage enhancement plotted against the independent variable time.[19]

DCE-MRI, besides breast tissues, can also look into chest regions, especially on cardiovascular muscles. By injecting contrasts inside the patient, the contrasts will flow through different organs and highlight abnormal functions. This gives DCE-MRI the ability to produce high spatial resolution and is efficient in detecting scars in muscular tissue of the heart and

[19] Riham H. El Khouli, Adeline Louie, Case of the Season: A Giant Fibroadenoma in the Guise of a Phyllodes Tumor; Characterization Role of MRI, Seminars in Roentgenology, Volume 44, Issue 2, 2009.

subendocardial infarcts.[20] According to a study,[21] unrecognized myocardial scar detected by DCE-MRI are strong indicators of heart attacks which could result in cardiac death. They also provide feedback on the myocardium that is extremely helpful to inform the patient about their heart condition. What is worth noting is that damages on those tissues can occur without the patient experiencing pain. Through DCE-MRI, physicians can identify myocardial infarction by comparing the contrast in the left ventricular (LV) mass (figure 10). Some may think that these infarctions are better than cardiac arrests since patients are not in pain, but this situation is actually more dangerous since patients would not reflect any abnormal feelings to their physicians, thus a specific scope (in this case DCE-MRI) on the subendocardial region may not be conducted.

Figure 10. DCE-MRI image showing a tear on the inferior and inferoseptal walls indicated by the arrow.[22]

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[20] Evrim Bengi Turkbey, David A. Dombroski, Cardiac Magnetic Resonance Imaging: Techniques and Clinical Applications, Seminars in Roentgenology, Volume 44, Issue 2, 2009.
[21] R.Y. Kwong, A.K. Chan, K.A. Brown, et al. Impact of unrecognized myocardial scar detected by cardiac magnetic resonance imaging on event-free survival in patients presenting with signs or symptoms of coronary artery disease Circulation, 113 (2006), pp. 2733-2743.
[22] Evrim Bengi Turkbey, David A. Dombroski, Cardiac Magnetic Resonance Imaging: Techniques and Clinical Applications, Seminars in Roentgenology, Volume 44, Issue 2, 2009.

Another application of MRI in cardiology is Cine MRI. It can be used to assess the left ventricular mass. Unlike traditional RF pulses, Cine MRI uses a technique called steady-state free precession (SSFP) sequences. Instead of having the magnetization die out between pulses, SSFP applies the pulse so rapidly that the tails of each pulse begin to merge (figure 11). The magnetization vector has two components. One in the xy-plane and the other in z-plane. The excitation states then flip each other, with the spontaneous regrowth of those two vectors creates a steady-state equilibrium. Because SSFP has short interval of sending pulses, this intrinsically brings faster imaging speed. However, the quality of the image depends on the homogeneity of the magnetic field.[23]

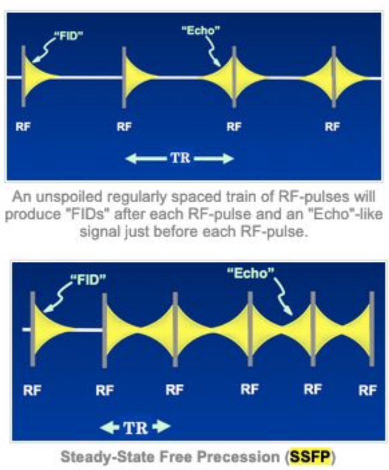
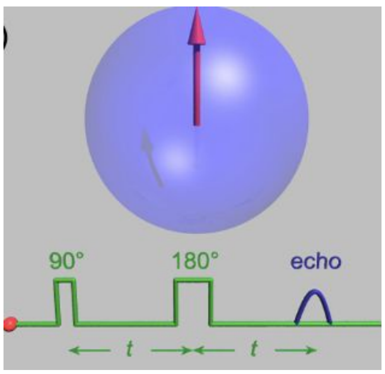


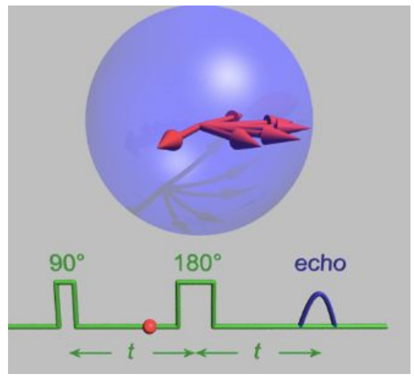
Figure 11. Tails of the "FIDs" and "Echoes" from RF pulses merge to produce continuous signal of varying amplitude.[24]

Because of the gradient used in MRI, the magnetic field within a region is slightly different. This means some magnetic moments of the nuclei will precess faster than others. By

[23] "Steady State Free Precession." *Cardiac MRI*, https://www.med-ed.virginia.edu/courses/rad/cardiacmr/Techniques/SSFP.html.
[24] "What Is Meant by Steady-State Free Precession (SSFP)?" *Questions and Answers in MRI*, http://mriquestions.com/what-is-ssfp.html.

hitting the region again with an 180-pulse, it flips the magnetic moments so now the slower precession is closer to alignment and the faster precession is further away.[25] This will cause the individual moments that are decoherent to be focused again (figure 12).





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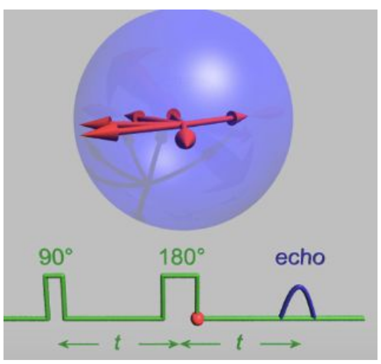

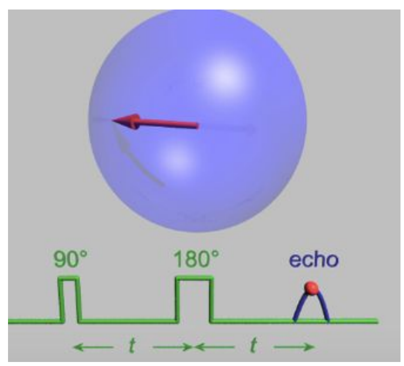

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Figure 12. A)Average magnetic moment of spins in a group that are stationary on average. B)Variation of spins due to gradient. C)After a 180°-pulse the slower spins are now closer to alignment. D)Refocusing of the spin that appeared to be stationary on average again.[26]

[25] Hammer, Mark. "MRI Physics: Pulse Sequences." *XRayPhysics*, 2014, http://xrayphysics.com/sequences.html#se.
[26]Morley, Gavin W. "Spin Echo." *Wikipedia*, Wikimedia Foundation, 16 Nov. 2019, https://en.wikipedia.org/wiki/Spin_echo#/media/File:SpinEcho_GWM_stills.jpg.

Since the invention of magnetic resonance imaging, physicians and patients have been able to see inside of and analyze complex body structures. This technology creates high quality contrasts between fat, water, and soft tissues. It is not radioactive compared to other technologies that produces similar images such as Computer Tomography, Positron Emission Tomography, and Single Photon Emission Computed Tomography. This brings patients certain assurance, especially those in long term treatment, knowing that they are not exposed to radioactivity frequently.

Just like Cine MRI, however, where faster imaging process does mean lower imaging quality, MRI in general have trade offs in safety. The technique itself is safe, but other circumstances may jeopardize the safety of patients and physicians. The room where MRI is conducted is an enormous magnetic field. If any metal is brought in the vicinity, it will most likely attract that object to fly across the room. In addition, if a pacemaker is implanted inside the patient, it may be deadly to patients as they will be pulled towards the magnets and experience damage to the heart. With that being said, there are MRI-safe pacemakers making it possible for those patients to have an MRI. As discussed in case studies, MRI is very effective in detecting subendocardial infarcts. Allowing patients with existing heart condition to undergo further cardiac imaging helps dramatically to diagnose and create adequate treatment plans.

In the future, there could be MRI machines where it is still prohibited to bring any metal objects into the room, but the machines will alert the staff so that the danger can be handled properly and quickly. In other words, future scientists may be able to develop MRI machines that do no require the magnet to be running all the time and can be toggled relative easy. Or in the case of pacemaker, the medical industry will make instruments that are typically metal to be MRI compatible. Humans have spent all their time looking for ways to benefit people they care about and always will. Regardless if those exact products are invented, hopefully this imaging technique used in the fields of inflammation, cardiology, oncology and other fields will not be the stopping point for medical, research, and other academic communities; that MRI technology advances as humans continue to explore on the road of unknown.

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