

USING HIGH-DOSE, GADOLINIUM- ENHANCED MRI STUDIES IN THE CLINICAL SETTING

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INTRODUCTION

Since the advent of magnetic resonance imaging (MRI), there has been a continuous effort to improve the quality of the images produced by this imaging medium. Many of the efforts have been aimed at improving the software that exists in order to address problems such as *motion artifacts* and *signal void*. Enhancing the images through the use of contrast agents is a technique that has long been employed in MRI. Recently, more attention has been focused on the effect created by varying the dose rate of MRI contrast agents. This article will review several studies that address this issue in particular, with special emphasis given to the use of high doses of contrast agents.

CONTRAST AGENTS: CONTRAST-RELATED RESEARCH

The contrast agents used for MRI procedures are gadolinium chelates administered at a rate of 0.1 mmol/kg body weight.¹ Gadolinium has been widely used without the stigma of serious side effects for the majority of patients. The same cannot be said for the iodine-based contrast agents used in other specialty imaging areas, such as CT. A large portion of the population exhibits side effects to iodine-based contrast agents, ranging from mild to severe. An example of a mild side effect to an iodine-based contrast agent is the development of hives; serious side effects include respiratory problems to the point of anaphylactic shock. However, there has not been any reported case of serious side effects to the contrast agents that are

used to enhance MRI procedures.²

In the early years of MRI, gadolinium was administered solely through hand injections that used intravenous (IV) setups for delivery. The technologist would perform a predetermined set of scans before the contrast agent was introduced, and then the gadolinium would be administered via the IV setup. Further scans would then be performed to determine if the contrast agent would delineate any pathology. As mentioned earlier, there is a recommended level of gadolinium for the patient, determined by the patient's weight. Once the gadolinium was administered, the post-contrast scans would be performed immediately to avoid having the contrast "wash out" of the patient's system, negating the effect of the contrast material.

With the evolution of higher levels of software, more complex procedures are being performed than ever before in the MRI suite. Angiograms, venograms, and other examinations typically performed in the special procedures angiographic suite are now being successfully conducted using MRI. To be successful, many of these special procedures require higher doses of contrast agents that are introduced at a faster rate than possible through hand injecting. To that end, *pressure injectors* have been introduced to the MRI scanning rooms. Patients are still prepared with a typical IV setup for delivery of the contrast agent, but delivery of the contrast agent is often through pressure injectors to administer a large bolus in a rapid timeframe.

A pressure injector works with the computer system of the magnetic resonance imager. This injector is capable of delivering a predetermined amount of contrast agent at a predetermined time to guarantee optimal post-contrast imaging. The technologist uses a syringe to draw up the gadolinium, inserts the syringe into the pressure injector, and then connects the tubing from the pressure injector to the IV tubing. The technologist is also responsible for programming the pressure injector so the correct parameters are employed-including rate of delivery, amount of contrast used, and any delays that might be needed. Once the system is engaged, it will work with the MRI scanner to inject the contrast at the optimum time, ensuring that the images obtained will be gathered at the peak point of contrast administration. This ensures that the anatomy being examined will be imaged when the highest level of contrast

concentration is in the patient's body.

Research is being conducted to determine what effect increasing the dose of gadolinium will have on producing diagnostic images in the MRI arena. The dose normally recommended, determined by the weight of the patient, is 0.1 mmol/kg. For high-dose, gadolinium-enhanced scans, doses at the rate of 0.3 mmol/kg, or three times the normal rate, are used. Some very interesting studies have been performed with clear indications that high-dose imaging is a beneficial approach with regard to diagnosing certain types of disease.⁴

Researchers in one such study² examined the effect of high-dose, gadolinium-enhanced MRI for diagnosis of meningeal metastases. In this study, 12 patients were imaged using both standard dose and high-dose gadolinium. The findings of the data collected from this study demonstrate the advantages of high-dose, gadolinium-enhanced MRI over standard dose imaging in the diagnosis of meningeal metastases. Confidence in the diagnosis of the patients during the high-dose phase of this study was higher than that for the standard-dose phase, based on several observations.

Initially, the standard-dose approach did not identify one of the patients who did in fact have the disease. Further, in two other patients, the standard-dose approach did not delineate the disease adequately. Once there was an introduction of high-dose gadolinium, the first patient's meningeal metastases were positively diagnosed, and the two other patients' disease was delineated more fully, which allowed for a more accurate diagnosis.² Given that no negative effects resulted from the increased dose of gadolinium, it is easy to see why the researchers concluded that this approach added value to the study.

Researchers in another study³ examined what effect, if any, increased doses of gadolinium would have on image enhancement at different magnetic field strengths. In the MRI suite, magnetic field strength is measured in units called *tesla* (*T*). The magnetic field will vary from scanner to scanner from very low-field strength, such as 0.2 tesla, to high-field strength, such as 1.5T. With this variable taken into consideration, these researchers also found benefits for the use of higher doses of gadolinium.

The main goal of the study³ was to compare the contrast between intracranial, contrast-enhancing, space-occupying lesions and the surrounding white matter obtained with low-field (0.2 T) and high-field (1.5 T) MRI and to find the contrast medium dose for low-field MRI that produces the same lesion-to-white matter contrast as that obtained with high-field MRI after the administration of a standard dose of the contrast medium.³ The 38 selected subjects for this study each suffered from intracranial metastases or high-grade gliomas.

One of the reasons behind designing this study was the fact that many of the magnetic resonance imagers that are located in the operating suites are lower in field strength. Field strength in MRI is a very impor-

tant variable because it affects the images produced and the ultimate enhancement of the pathology in question. For patients who are being scanned intraoperatively critical decisions must be made regarding future medical interventions. These decisions are based largely on the images produced in these scans. If a tumor does not enhance correctly, or to the fullest extent possible, then it is possible that a misdiagnosis could occur, and poor choices could thus be made with regard to surgical intervention and treatment.

Researchers from this study³ concluded that increased doses of gadolinium should be administered when patients are being scanned by a low-field MRI unit. The standard dose, 0.1mmol/kg body weight, was sufficient in the high-field, 1.5-T scanners for purposes of lesion-to-white matter delineation. However, when the lower field strength scanners were used, the standard dose of contrast was not adequate to thoroughly enhance the pathology.

In this study, the gadolinium dose was first doubled to 0.2 mmol/kg body weight to obtain images, and then ultimately tripled to 0.3 mmol/kg body weight. The images obtained with the double dose at the lower field strength were comparable to the single dose given in the higher field strength. Tripling the dose at the lower field strength was not found to provide notable improvement over doubling the dose. This information is very important when crucial decisions are being made with regard to patient medical intervention.³

The focus of another study⁴ was the use of expanded doses of gadolinium in the evaluation of the lumbosacral spine. The most widely used dose of gadolinium for examination of the lumbar area in the MRI setting is the standard dose of 0.1 mmol/kg, introduced intravenously. Images of the area are acquired before and after the contrast is administered to delineate the anatomy in the region and search for any pathology that might be present. In this study,⁴ the normal dose of gadolinium was tripled to discover what effect the increased amount of contrast might have on enhancement and delineation of anatomic structures.

A total of 12 research subjects were recruited for this study,⁴ and each of the participants presented with absolutely no symptoms of disease. Prospective subjects were extensively screened for prior back surgery or back trauma. Any subject with such a history was eliminated from the study. The median age of the 12 subjects was 25 years. Eleven of the 12 subjects completed the study. One of the participants withdrew due to problems with claustrophobia in the scanner.

After the tripled dose was administered to study participants, the resulting images showed increased enhancement in the facet joints, intervertebral disks, and structures within the thecal sac.⁴ Enhancement within these areas, particularly the thecal sac, is much less pronounced with the usual dose of 0.1 mmol/kg body weight.

Although the results of this study offered credible evidence of increased enhancement of the lumbosacral area with the tripled dose of gadolinium, a word of caution also became evident. That is, enhancement associated with pathologic processes must be distinguished from enhancement due to the triple dose of gadolinium. Thus, if the increased amount of contrast is incorporated into the protocol for examination of the lumbosacral region, radiologists in charge of interpreting the images need to be made aware of the increased dose to eliminate mistakes made during interpretation of the images. The authors of the study⁴ suggested that a possible solution to this problem would be to incorporate an initial injection of 0.1 mmol/kg body weight, acquire images, and then administer the triple dose of contrast and acquire images again.

Several abdominal studies have been conducted to search for a correlation between increasing doses of contrast agents in MRI scans and resulting image enhancement. Researchers in one such study⁵ used a dose-ranging approach in patients with focal liver lesions that had already been documented through the use of CT or ultrasound. The 30 patients selected for this study were divided into four different dosing groups and given a predetermined amount of gadolinium, depending on the group to which they were assigned. The dose range ran from very low to double the normal dose. The ranges were 0.025, 0.050, 0.1, or 0.2 mmol/kg body weight. All of the patients were scanned in a 1.5T MRI system.

Once again, the results of this study pointed toward the benefits of higher doses of gadolinium for examining patients in the MRI suite. The most prevalent finding was that the higher doses provided enhancement of images of normal liver tissue that was statistically significant. The researchers searched for enhancement increases through region-of-interest measurements. Examination of the liver lesions showed that enhancement increased with the increased contrast dose. However, there was not a significant level of improved enhancement of liver lesions. Overall enhancement, that was statistically significant, especially of the normal liver tissue, was the major finding of this study.⁵

In another study that examined dynamic enhancement of upper abdominal organs, 10 healthy male volunteers participated. The main thrust of this study was to discover optimum timeframes for imaging patients after the injection of contrast in the MRI setting.

Researchers in this study found that optimum visualization of upper abdominal organs occurred very quickly after contrast injection, usually in less than 25 seconds. For this reason, the researchers pointed out that scanning should begin very quickly after contrast injection and continue through the venous phase. The researchers recommended that injection parameters be standardized to capture arterial and venous enhancements, especially for the liver.¹

A secondary finding from this study,¹ consistent with that of other related studies, was also discovered. The 10 male volunteers had been scanned on two separate occasions. During the first scan, the researchers used a dose rate of 0.1 mmol/kg body weight. During the second scan, the researchers used a dose rate of 0.075 mmol/kg body weight. Although this is a very small incremental dose change, there were notable findings with respect to contrast-agent enhancement. The 25% dose reduction, although very small, did significantly reduce overall enhancement of the images produced. However, peak enhancement was not significantly reduced, except for the area of the liver.¹ Once again, these findings suggest that increased levels of contrast contribute to the successful collection of MR images.

The research being conducted to discover optimum levels of contrast introduction in the MRI arena is fairly new. This should come as no surprise, however, when we stop to consider how new MRI is in the medical imaging field. One of the biggest challenges for researchers in this area is to continually develop all aspects of image enhancement to the fullest extent possible. The role played by the contrast agent in successfully producing excellent MR images is one that is crucial and deserving of the attention it is receiving.

CONCLUSION

Research findings from the studies reviewed here were all in agreement regarding contrast agent administration. Because patients usually do not suffer side effects from the MRI contrast medium, there's no clinical reason to use lower doses. In addition, patients do benefit from the increased enhancement that occurs with the administration of higher doses of contrast agent. The findings of some of the studies cited here show that important diagnostic information would be missed without the increased enhancement due to administration of higher contrast doses. Because of critical decisions relating to medical intervention for the patient and long-term treatment success, the role of high-dose gadolinium cannot be overlooked. High-dose, gadolinium-enhanced MR images allow the physician to become a better diagnostician.

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SUGGESTED READING

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USING HIGH-DOSE GADOLINIUM-ENHANCED STUDIES IN THE CLINICAL SETTING POST TEST

Expires: July 15, 2009 Approved for 1 ARRT Category A Credit.

1. **The contrast medium used for MRI contains which of the following?**
 - a. Saline
 - b. Iodine
 - c. Gadolinium chelates
 - d. Heparin
2. **The contrast agent used for MRI frequently produces which of the following side effects?**
 - a. Hives
 - b. Vomiting
 - c. Breathing problems
 - d. None of the above
3. **The contrast agent used for CT is known to produce which of the following side effects?**
 1. Hives
 2. Vomiting
 3. Breathing problems
 - a. 1 only
 - b. 2 only
 - c. 1 and 3
 - d. 1, 2 and 3
4. **What percentage of the population has reported serious side effects from MRI contrast administration?**
 - a. Virtually zero
 - b. 10%
 - c. 20%
 - d. 50%
5. **How were contrast agents administered in the early days of MRI?**
 - a. Orally
 - b. Through inhalation
 - c. Through hand-injected IV setup
 - d. Through pressure-injected IV setup
6. **What variable is most influential with respect to the recommended dose of MRI contrast administration?**
 - a. Patient age
 - b. Patient disease process
 - c. Patient gender
 - d. Patient weight
7. **Technologists must select which parameters on the pressure injector?**
 1. Rate of delivery
 2. Amount of contrast delivered
 3. Start and stop time
 - a. 1 only
 - b. 2 only
 - c. 1 and 3
 - d. 1, 2 and 3
8. **What dose of gadolinium is most widely used in MRI examinations?**
 - a. 0.01 mmol/kg body weight
 - b. 0.25 mmol/kg body weight
 - c. 0.1 mmol/kg body weight
 - d. 0.3 mmol/kg body weight
9. **What does the term tesla refer to?**
 - a. Brand of contrast
 - b. Strength of the magnetic field
 - c. Number of contrast injections given
 - d. Brand of pressure injector
10. **The strength of the magnetic field**
 - a. does not influence image outcome.
 - b. influences image outcome.
 - c. uses more gadolinium.
 - d. should always be increased based on the amount of contrast agent injected.
11. **Increased contrast dose in MRI has been found to be beneficial in the enhancement of images obtained**
 - a. with low-field scanners.
 - b. with high-field scanners.
 - c. only of the extremities.
 - d. only of the vertebrae.
12. **Increased contrast dose in MRI studies leads to increased**
 - a. patient cost.
 - b. scan time.
 - c. patient discomfort.
 - d. image enhancement.
13. **What is the rate of contrast media given for high-dose studies?**
 1. Double the standard dose
 2. Triple the standard dose
 3. 10% more than the standard dose
 - a. 1 only
 - b. 2 only
 - c. 1 and 2
 - d. 1, 2 and 3
14. **Increased enhancement of normal structures could lead to**
 - a. a false diagnosis of a disease process.
 - b. organ failure.
 - c. longer scan times.
 - d. decreased organ function.
15. **How soon should scanning begin after contrast administration?**
 - a. Before 25 seconds pass
 - b. Before 10 seconds pass
 - c. After 1 minute
 - d. After 5 minutes
16. **Patients who receive higher doses of contrast media in the MRI suite experience which of the following?**
 - a. Increased nausea
 - b. Increased incidence of hives
 - c. Increased levels of anxiety
 - d. None of the above

- 17. What type of scanner is used most prevalently in the operating suite?**
- High-field
 - Low-field
 - 4.0-tesla system
 - No scanners are used in the operating suite.
- 18. Contrast agents help delineate what in MRI examinations?**
- Tumors
 - Disease processes
 - Metal-induced artifacts
- 1 only
 - 3 only
 - 1 and 2
 - 1, 2 and 3
- 19. One way to overcome false diagnoses due to increased enhancement provided by high-dose contrast studies in MRI would be to**
- not perform the study in the first place.
 - tell the patient that they are having a high-dose study.
 - educate the doctors about the differing enhancements.
 - give the higher dose in two different injections.
- 20. High-dose contrast studies in MRI examinations provide**
- increased overall enhancement of the images.
 - increased enhancement of disease processes.
 - increased enhancement of normal anatomy.
- 1 only
 - 2 only
 - 1 and 3
 - 1, 2 and 3



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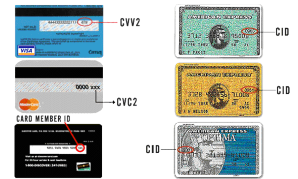
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