Incidental Findings on Research Functional MR Images: Should We Look?

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Use of the Lowest Necessary Radiation Dose

Radiologists are taught that CT with low radiation doses is morally and ethically justified provided that this technique produces images adequate for diagnostic purposes. CT accounts for a large proportion of overall radiographic exposure to the patient population. In this issue of the AJNR, Lev and colleagues address an important, though often ignored, topic. They carried out a controlled study of brain CT with mAS lower than that of standard doses. This topic is not discussed—can we even reduce the dose for soft tissue details on CT scans? A few cases without pathologic findings are shown.

For decades, neuroradiologists have welcomed the anatomic advances of many new techniques. We accepted physics theories and vendor advice that signal-to-noise concerns justify using recommended CT dose rates. It is brave of Lev et al to challenge dose rates commonly used for brain CT, yet the basis for lowered doses exists from scientific cadaver data (1).

Image conspicuity for brain structures such as gray and white matter is in a category of “low contrast.” For high-contrast CT used in the imaging of nasal sinuses (2–4), cervical spine CT for bone, and even CT angiography for vasculature, conspicuity of important structures is already notable. Sinus CT is now being performed with exposures as low as 20 mAS. Although some sinus CT has decreased to 20% or less of the dose previously used, Lev et al have reduced the cranial dose by 50%. This is an excellent start.

Cranial CT doses were lowered for imaging sinuses as early as 1991 (5) and have stood the test of time. Nevertheless, many neuroradiologists do not pay attention to the doses used in their own CT suites. CT technologists usually receive application training from CT vendors. Vendors do not like to demonstrate routine work at the minimal dose, because cases with more noise on images will be presumed to show a vendor’s product to be inferior. CT vendors provide the blueprint for technical operations regarding dose rates for CT, which is analogous to tobacco manufacturers being responsible for public health programs to prevent smoking.

It is important that neuroradiologists adopt an attitude that CT vendors will always recommend doses that are higher than those required for minimally acceptable images. This applies to fluoroscopy as well as CT. Unpublished experience with two different digital subtraction angiography manufacturers’ neuroangiography suites found that the “low-dose” fluoroscopy default button is really in a range of “mid to high dose.” Mid- and high-dose buttons were closer to maximal. Only after pleading and cajoling did the companies spend 1–2 full days of service engineering time to lower the fluoroscopy radiation dose and enhance the imaging chain to compensate for the change. This activity provided a reduced dose to about 20% of original “low dose” and allowed proper visualization for most angiographic fluoroscopy. This makes a great difference for total radiation exposure for patients undergoing procedures, including long and repeated interventional sessions that cause hair loss a few weeks later.

Lev et al’s results indicate the clinical feasibility of this low-dose technique. For a start, low-dose CT could work well for the diagnosis of hydrocephalus, subdural hematoma, and gross mass effects. Further study is needed to determine the diagnostic utility of low-dose cranial CT: we need to establish both obvious and subtle pathologic signs to determine when CT should be carried out at such reduced radiation doses. This presumably will come with a subsequent publication by that group.

Nearly two decades ago, as MR imaging was developing and then advancing rapidly, many predicted that CT would become obsolete because of its use of radiation exposure and less fine detail as compared with MR imaging. Nonetheless, CT advancement in recent years has been phenomenal, and because of the ease of conducting extensive CT studies in seconds, CT is now chosen over MR imaging for certain indications. It is imperative that attention be paid to CT dose rates. Dose rates need to be minimized to meet the first criterion of radiology: to use the lowest radiation dose necessary to produce the best possible image. We need to be able to tell our patients, our risk management committees, and ourselves that the lowest dose can and should be used. Dr. Lev and colleagues go a long way to provide a new attitude and safer environment for our patients.

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References
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In the Marx brothers movie, A Day at the Races, Margaret Dumont, in the role of a wealthy matron, praises Groucho as the one of finest doctors she has known, saying, “Why, I didn’t know there was a thing the matter with me till I met him.” Although radiologists frequently find themselves in a similar role, “incidental findings” present difficult medical and ethical questions when they appear on research imaging studies.

This is, of course, not a new problem. Even a cursory search with the keywords “incidental findings” will direct you to numerous articles. They will cover a range of topics such as sinus MR findings, cervical spine abnormalities shown on dental radiographs, and nephrolithiasis disclosed on emergency CT scans (1). In daily practice, physicians who review screening studies for cardiac calcification or lung cancer must make a decision whether they will even look at the soft tissues of the mediastinum or upper abdomen.

What brings this subject to the forefront is the expanding role of functional MR imaging (fMR imaging) for neuroscience research. This technology has proved to be a powerful tool for investigators who study brain function, and it has captured the interest of the general public. These studies, however, present some potential pitfalls, because they make high-resolution MR images of apparently healthy subjects the responsibility of investigators who may not have formal training in image interpretation. Although obtaining these images is effortless, management of the images presents some difficult choices, with significant implications for the subjects and the researchers.

Because these functional studies require advanced MR systems with powerful gradients, there is always the option to create high-quality structural images. Some limited T1-weighted images are always acquired for coregistration of the functional data, but these studies usually do not include fluid-attenuated inversion recovery (FLAIR) or T2-weighed images. The question that each research center must deal with at some level is whether a radiologist should review some, all, or none of the images. And if the investigator to have the studies reviewed, who would be responsible for contacting the patient or his/her physician when there are abnormal but often equivocal findings in terms of clinical significance? From a practical viewpoint, how will they even get a radiologist to review these studies at a time when radiologists are in short supply?

Do not expect to find the answers to these questions here. I can only offer the evidence, defend our rationale, and describe the approach that has been used at our institution. First, the data. Although there are fewer than a dozen articles on this topic, large and small studies of young and old all report medically significant findings in 1–2% of their subjects. What justifies medical intervention is not simple to define, but nearly all would agree that findings of a CNS tumor or aneurysm deserve further attention. Katzman et al (2) reported two confirmed brain tumors and one unconfirmed in a study group of 1000 largely young but all asymptomatic volunteers imaged with MR. Two other articles—one by Yue et al (3) and another by Mirza et al (4)—have more diverse subject groups, yet the incidence of significant findings again fall in this range of 1–2%. An article by Lubman et al (5) included 98 healthy controls and 242 subjects with psychotic mental illness. Although there were more findings in those with psychoses, particularly those with symptoms for >2 years, the incidence of significant findings in all groups was again 1.1%. A review of our own experience with 198 fMR imaging examinations with 97 controls and 101 subjects revealed three subsequently confirmed cerebral aneurysms, for an incidence of significant findings of 1.5%. One important feature common to all these studies is that a neuroradiologist reviewed the images.

Accepting that range of 1–2% as the expected incidence across the board, what should be done with these abnormal imaging findings? Kim et al (6) recommend that all research studies involving pediatric subjects should involve a radiologist who would be expected not only to identify the findings, but also to ensure that there is appropriate follow-up. Although such an approach is probably not feasible at all centers, there should be a defined pathway for dealing with these abnormal imaging findings because some of these unexpected results are not appropriate to discuss casually with the subject, particularly when his or her medical history is unknown. There are also records and images that need to be filed in a fashion that protects privacy but allows for retrieval.

In the spirit of disclosure that we all hope pervades medical publications, I must admit at this point that I am not a dispassionate observer in this arena. Not long after finishing the review of our own experience with incidental findings, I volunteered to serve as a subject for a study we were finishing up for this past ASNR meeting. With no small degree of irony, one of our very skilled MR technologists found a cerebral aneurysm on my images. Am I grateful for this discovery of an asymptomatic aneurysm? Absolutely. Did I have surgery? Wouldn’t you? Consider how you might feel, assuming that you could, after an aneurysm ruptured a year from now and it was evident but not recognized on a retrospective review of a research imaging study? I bring this to light largely to help put these questions into some perspective and emphasize that this is not some abstract concept that does not require your attention just now.

It is not entirely clear what the legal obligation of the investigator to the subject might be, because the traditional patient-physician relationship does not exist with its associated benefits and obligations. The
article by Illes et al (7 very nicely reviews the scope of this problem and suggests that informed consent might be the appropriate vehicle to limit the expectations of the subject. Illes et al use a consent in which it is made clear that images are not reviewed by a radiologist and the study they undergo is not equivalent to a clinical imaging session. In one section of the informed consent quoted in the article, however, they state, “The investigators for this project are not trained to perform radiologic diagnosis. . . . However, on occasion the investigator may notice a finding on a MR imaging scan that seems abnormal.” This is the standard practice at many centers, but I wonder whether the subjects find this ambiguous? It seems reasonable that they would infer that, if there is no follow-up, their imaging findings must have been normal. What about those that are abnormal for which findings are too subtle to be noticed in a casual review of the images? The literature presents compelling evidence that there will be many significant imaging findings that will not be detected by an investigator who is not an experienced imager. For example, small meningiomas, which are among the most common CNS tumors, are often very difficult to discern on unenhanced T1-weighted images.

Because there are no obvious legal guidelines, it would seem appropriate to respond to the expectations of the subjects. Although some assume that the subjects in fMR imaging studies are motivated solely by their interest in forwarding medical research, in some cases the possibility of getting a “free” MR image of the brain is a powerful motivation. For example, as part of a study at our institution on aging and memory, subjects were asked about their motivation for volunteering for the study during a structured interview. Among 23 healthy controls determined to be cognitively normal on neuropsychological testing only half endorsed being “interested in helping research” as a key factor. In this sample, many said they wished to enroll because they were either concerned about their own memory or in response to a family member’s concern about their memory. Although it is also tempting to assume that these incidental findings are less of an issue in controls as compared with subjects, in our small experience two of the three aneurysms (or three total, including me) were in the asymptomatic control group. In the study by Katzman et al, all the patients were young and asymptomatic, yet they found two brain tumors. Perhaps controls are more likely to volunteer for fMR imaging if they have some ill-defined concern that there is something wrong? For whatever reason, significant findings occur in all groups, and there is often a tacit expectation that someone with training will look at the subject’s image.

It is worth considering in passing the question that underlies the whole topic: are we really adding quality or years of life to these subjects by making the early diagnosis of brain disease? How does this differ in principle from the “screening CT” scans, which have had a generally cool reception by the medical community? For example, it would seem that, at this time, even the neurosurgical community is not quite sure of the optimal approach to small, incidentally identified cerebral aneurysms. Does this uncertainty absolve us of responsibility? There is, however, at least one fundamental way that this situation differs from screening studies. It is the researcher who is asking the subject to get in the MR system. In this circumstance, we should meet the subjects’ expectations or advise them in advance that there is no diagnostic value attached to their participation in the study.

In fact, many research centers are currently dealing with these questions on a case-by-case basis, depending on what is seen on the image. Is it reasonable to use an approach in which the image is sent to a radiologist only after being screened and considered abnormal by the investigator? This approach presumes that the task of separating normal from abnormal findings is simple, yet from practice I would argue that this step is often the most difficult task for an imager.

The approach used at our medical center was established because many of our subject groups have underlying diseases such as multiple sclerosis, dementia, traumatic brain injury, cancer, or mental illness, and we assumed at the outset that the incidence of abnormalities might be higher in these groups. What proved to be of interest and surprising to me over time was the equally high incidence of significant findings in the “normal” control groups. Once the decision was made to have all images reviewed by a neuroradiologist, we also decided to obtain either a FLAIR or T2-weighted image, in addition to their T1-weighted study needed for the coregistration of the fMR image. All of the aneurysms in our experience were evident on the T2-weighted or FLAIR images. These images are read weekly, usually in a conference setting with the investigators. Any previous images are available, and the reader has access to the participant’s age and, after an initial blinded review, to some clinical information regarding the status of the subject. The reading is then transcribed and after approval by the neuroradiologist it is included in participants’ research file and in a password-protected data base of image readings. Subjects are asked at the outset whether they wish to have a copy of their MR imaging placed in the hospital archives for future medical reference. As part of the informed consent process, participants are asked to name their primary care provider and give consent for the investigators to notify their provider if any findings are evident that merit follow-up care. Participants also are asked to give consent to having a note regarding the findings placed in the hospital record. At these weekly meetings plans for follow-up are decided, and they may include the notification of the participant and/or their
designated care provider or a request for further imaging such as contrast enhanced images or MR angiography.

What incentives can be used to engage the radiologist? Apart from the perceived obligations to the subject group, there should be financial and academic incentives. This topic is again well dealt with in the article by Illes et al, and we use a combination of academic involvement in these research projects and funding that reflects the time needed to make this a workable arrangement.

There are many approaches currently used by the research community to address, or not address incidental findings. Although this variation is likely to continue, centers that use structural imaging only as a localizing framework should advise the subjects of this in the informed consent process; however, because the evidence makes it clear that significant findings will be encountered in 1–2% of their cases, research centers should develop a consistent approach that involves trained imagers so that these subjects will have the opportunity to receive appropriate follow-up imaging or care.

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