

Digital Forensics and the *American Journal of Neuroradiology*

Peer review doesn't necessarily say that a paper is right. It says that it's worth publishing.

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In the media, the term “digital forensics” usually refers to investigations regarding the mining of data stored in digital fashion. Many government and private firms specialize in this activity. In the context of this short commentary, I will use the term “digital forensics” to mean the activity of discovering unintentional or fraudulent alterations of images (both static and video). Alteration of images is an everyday fact and is commonly used by the popular media. Historically, photographs have been “doctored” for a long time, and many of them are now regarded as art (just look at those from Mathew Brady and Man Ray!).

Why is the *American Journal of Neuroradiology* (*AJNR*) interested in digital forensics? Immediately after I became Editor-in-Chief, one of our astute reviewers noticed some unusual “cloning” in images submitted to *AJNR*. After some investigation, which involved obtaining the original figures, one of our Senior Editors and I came to the conclusion that these alterations were innocent and did not alter the authors' results. Alterations of images in scientific journals are common. The most famous one involves the illustrations published in *Science* by the South Korean scientists Woo-Suk et al,¹ showing lines of stem cells that did not exist. It is this incident that led to some journals now asking for specific details regarding the contributions of each author when a manuscript is submitted. *Science* is not the only journal to have had such articles published. The *Annual Report 2006* of the Office of Research Integrity from the Department of Health and Human Services lists similar instances appearing in the *Journal of Biologic Chemistry*, *Blood*, *Cancer Research*, *Mutation Research*, *Molecular and Cellular Biology*, and *Cell*, among others.² The same office noted that in 1990 less than 3% of scientific frauds involved images, while by 2001 this number had climbed to 44%. Mike Rossner, Executive Director of the Rockefeller University Press, has been quoted saying that 20% of manuscripts accepted by one of their publications, the *Journal of Cell Biology*, probably contained at least 1 image that had been digitally manipulated and that 1% of all images published may be fraudulent.³

Any person with enough time on his or her hands and who owns Photoshop (Adobe Systems, San Jose, Calif) or any other such software can alter images. Image manipulation may be “authentic,” and that, in my opinion, includes deleting identifiers, changing contrast and brightness to make the image(s) more pleasing, cropping edges, alignment, and some “cleaning.” How much of an image may be altered without fundamentally changing its true nature is debatable. Sometimes, changes of 25% or more do not affect the value of an image, while other times, changes as little as a few pixels may significantly change an image. There is considerable discussion

about how many shades of gray the human eye can distinguish (I have seen numbers quoted from as low as 16 to as high as 500). Some say that we are better at distinguishing different colors than shades of gray. Regardless, computers are able to detect very small changes in grays and contrast (far better than we humans). Because computers do not actually “look” at the pictures but rather analyze the numbers that correspond to each pixel and its depth, alterations are easier to discover. Commercial and free software used for this purpose is available (ie, Foveapro, Reindeer Graphics, Asheville, NC; ImageJ, public domain: <http://ori.dhhs.gov/tools>; and ORI Forensic Tools, public domain: http://ori.dhhs.gov/tools/data_imaging.shtml). Commercial publishers have also developed or are developing similar but more sophisticated products. *AJNR* is produced by Cadmus Communications, which now offers a program that detects image manipulation. Regardless of who designed the program, these are capable of “deconstructing” an image and detecting alterations in previously fused layers such as those found in TIFF (tagged image file format) images and other formats. Obviously, the significance of the findings is left to human judgment. These programs only direct the editorial staff by highlighting tampered regions. Additionally, unless a comparative figure is available, alterations, duplication, and plagiarism cannot be detected.

As an editor and a radiologist, I recognize the need to enhance contrast and detail in images; however, I am also worried about publishing images that will later prove to be false. For the benefit of our authors and readers, this is what I consider acceptable in regard to digital image manipulation:

- changing image size and resolution as required in the “Instructions for Authors”;
- globally adjusting contrast and brightness (as long as no parts of an image are completely masked by them);
- blocking or erasing patient/institutional/manufacture identifiers;
- minimally “cleaning” unwanted noise in the background;
- aligning an image that is tilted;
- cropping unnecessary surrounding black space.

All cloning, whether it was done to delete or enhance a part or parts of an image, is viewed as suspicious. No specific feature within an image may be enhanced, obscured, moved, removed, or introduced. Should alterations be suspected, the images will be sent to our printer who will analyze the changes. We will then contact the corresponding author and ask for the original unadulterated image files. Inability to produce the original data is generally enough to reject a manuscript.⁴ The editors will then judge the significance of these alterations. The authors may be asked to return to their original illustrations or may be allowed to use the altered one(s) only if we consider that the impact of the changes is not important. If the altered images are used, this should be pointed out and explained in the corresponding legends. If the editors conclude these changes were made with the intent of fraud, the submitted manuscript will be immediately rejected and coauthors and superior authorities will be notified of this action. If the investigator(s) received Public Health Service funding, a report to the Office of Research Integrity must be made.⁵ Violation of the basic tenets of scientific integrity, that is intellectual hon-

esty and accuracy, will not be tolerated by the editorial staff of the *AJNR*.

After the South Korean stem cell scandal, a survey showed that 8 of 10 Korean investigators were not aware of the "Declaration of Helsinki."⁶ This declaration reflects the policies of the World Medical Association with respect to research and states that both authors and publishers have ethical obligations that include preservation of the accuracy of the results in any investigation. Because we are an image-driven specialty and journal, we need to abide, in the most rigorous fashion, by the above-mentioned principle if we want to retain our credibility.

Mauricio Castillo
Editor-in-Chief

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EDITORIAL

A New Era in Neuroradiology: Ex Vivo Validation of In Vivo Imaging Research

In an intriguing article in this issue of the *American Journal of Neuroradiology* on diffusion tensor imaging (DTI) and brain abscesses, Gupta et al¹ have elevated the field of neuroradiology to a more sophisticated and erudite level. These authors set new standards for the investigational analysis of novel imaging techniques and their application to patient care. Our attention is directed not only to what lesions DTI and fractional anisotropy (FA) can diagnose and how these techniques can be used in treatment monitoring but also to the molecular basis for this diagnosis and treatment response and the ex vivo validation. These authors show us that we should no longer be content with the use of conventional images to diagnose brain abscesses (by the display of thin ring enhancement in lesions that demonstrate high signal intensity centrally and low signal intensity peripherally on T2-weighted imaging, low signal intensity centrally on T1-weighted imaging, and high signal intensity centrally on diffusion-weighted MR imaging [DWI] with matching low signal intensity on apparent diffusion coefficient [ADC] maps indicative of restricted fluid motion) but that we must also use these latest imaging techniques to expand our understanding of the molecular basis and the tis-

sue microstructure of this pathology.^{1,2} This greater comprehension, bolstered by the results of confirmatory ex vivo investigations, should not only increase our confidence in the imaging diagnosis of brain abscess but should also aid clinicians in the development of new treatment strategies.

So just what exactly did these investigators do? They examined by DTI 24 consecutive patients with brain abscesses and then quantified the FA in the central portion of the brain abscess.¹ After sonography-guided neurosurgical aspiration of the pus from the abscess cavity, the neuroinflammatory molecules from the aspirate, including tumor necrosis factor- α , interleukin1- β , lymphocyte function associated molecule-1, and intercellular adhesion molecule-1, were analyzed and quantified. Increased FA was found to be correlated with the presence of these neuroinflammatory molecules, leading the authors to suggest that this increased FA was a reflection of an upregulated inflammatory response in brain abscess.¹ However, these authors did not stop their investigation there. The beauty of their research was that they went 1 step further and confirmed their results through ex vivo assays. They induced neuroinflammatory molecules in Jurket cell lines by exposing them to heat-killed *Staphylococcus aureus*.¹ They then performed DTI and obtained FA measurements at 4 time points (1, 24, 48, and 72 hours) on both *S aureus*-treated as well as nontreated Jurket cell lines and confirmed that increased FA correlated strongly with the presence of these neuroinflammatory molecules.¹ They concluded that the increased FA was due to the structured orientation of neuroinflammatory cells in the abscess cavity, an environment induced by the upregulation of these various adhesion molecules on the inflammatory cells.¹

This theory certainly seems to make sense if one reviews the mechanism of abscess formation in the brain. As briefly summarized by Gupta et al,¹ it is thought that the presence of a bacterial organism in the brain such as *S aureus* activates glial cells, which then cause proinflammatory molecules to be secreted such as tumor necrosis factor- α and interleukin1- β , which subsequently influence the expression of numerous cell adhesion molecules, known as CAMs, located on the wall of the endothelial cells. Included among the CAMs are intercellular CAMs, vascular endothelial CAMs, and platelet-endothelial CAMs.^{1,3-5} The upregulation of these CAMs on endothelial cell walls leads to adherence of inflammatory cells such as neutrophils and to the opening of the blood-brain barrier and subsequent extravasation of these peripheral immune cells, which then target the infected area.⁵ A brain abscess develops in this milieu of immune activity and inflammatory response and, as a result, assumes a structured microenvironment due to these immune cells and neuroinflammatory molecules. Although many investigators, using DWI and ADC values, have drawn on this feature of a structured microenvironment to help distinguish bacterial brain abscesses from either cystic necrotic tumors or from fungal or parasitic brain abscesses^{2,6-11} and to aid in treatment monitoring,¹² the use of DTI and FA to make these distinctions is just now emerging.¹³ Even more novel is the exploration of the rationale behind these distinctions provided by FA.

The authors then are to be congratulated that they have provided us with ex vivo evidence to support their hypothesis relating FA to the upregulation of various adhesion molecules