ogy and the *American Journal of Roentgenology*) use HighWire and entrust their archives to LOCKSS. Our readers can be assured that the digital contents of *AJNR* are being adequately preserved for future generations.

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EDITORIAL

Randomized Vertebroplasty Trials: Bad News or Sham News?

The randomized trials on vertebroplasty treatment of painful spinal fractures by Kallmes et al[1] and Buchbinder[2] et al in the August 6, 2009 issue of the *New England Journal of Medicine* and widely reported in the popular press[3] deserve further comment.

I have performed well over 1000 vertebroplasties during a period of 9 years. I have personally treated numerous patients with osteoporotic and malignant compression fractures who were either bedridden or otherwise so limited by their pain that they became dependent on others for their daily activities. In virtually every case, vertebroplasty immediately reduced their pain and brought them to a level of function that conservative therapy would have taken at least months and several refills of narcotics to achieve. Consequently, I was surprised to see reports of these trials widely circulated in the press and to hear that referring physicians and patients may, therefore, now be reluctant to consider vertebroplasty.

When I saw the presentation of the data from a preliminary "sham" control study at a medical meeting a few years ago, I noted that the patients who had received the vertebroplasty procedure rather than the placebo (sham) procedure received minimal injections of polymethylmethacrylate (PMMA) compared with what I and others with good results typically inject. I recall others making comments on this point and on the ethics of doing such studies. I had not expected to see more of these studies because I considered vertebroplasty a "decided" matter until now.

I know from experience that the volume of cement necessary to restore axial integrity at virtually every level of the spinal column differs according to the shape, volume, and level of the vertebral body. After reading the research studies written by Kallmes et al and Buchbinder et al, my concerns of a few years ago were revived. Because there are no published post-PMMA injection images of vertebrae in the Kallmes study, I cannot conclude that the cement injections performed by this group of physicians on 68 of 131 selected patients at 11 different medical centers are anything other than minimal. By injecting only 3 mL of PMMA, the surgeons in the study of Buchbinder et al virtually guaranteed failure in all cases except fractures of the upper thoracic vertebrae. The study of Buchbinder et al of 78 patients did not give details on the spinal levels treated, so the reader is left to assume that fractures of the midlumbar region through T10 would have been most commonly encountered as is typical in most practices of experienced surgeons. Three milliliters of PMMA is generally insufficient to restore axial integrity in any of the levels that Buchbinder et al would have commonly encountered. Therefore, the study of Buchbinder is merely a comparison of nought to nought.

Second, a higher proportion (63% versus 51%) of patients who received the sham procedure in the Kallmes et al study correctly guessed the type of procedure by 14 days, and 43% of the patients who had received the sham procedure "crossed over" to get the real procedure. Notably, only 12% crossed over in the opposite direction. If the real procedure and the sham were truly equivalent, then such a lack of confidence in the sham procedure on the part of the patients who suffered the pain of the procedure—whether it was a sham or not, both types of procedures caused pain and discomfort—would not have been evident. These patients must have been thinking, "Why should I suffer another sham procedure when I know from my experience that relief of my compression fracture pain, which brought me here in the first place, will not be satisfactory?"

Third, reading of the study of Kallmes et al also revealed that enrollment of 250 patients with sufficiently painful compression fractures was an initial goal, but for numerous reasons (eg, 368 patients with suspected tumors and 704 patients who had either refused to participate or who had "other" reasons were excluded), only 131 patients were actually enrolled, thereby lessening the power of the study. There is, of course, no word as to how the group of 1072 nonenrolled patients was eventually treated.

In a busy practice in any major hospital, commonly more than 131 patients with painful compression fractures, due not only to osteoporosis, to which this study was limited, but also due to tumors and trauma that are not even addressed by this study, will be treated by the surgeons of that practice during a fraction of the time required to complete the Kallmes study. The experience of the surgeons (eg, as described by Kobayashi et al[4] and others[5-7]), the referring primary care physicians, the patients, and the caregiving family members is quite different from that indicated by the study of Kallmes et al.

I fear that this common experience will be ignored by the newly created Federal Coordinating Council for Comparitive Effectiveness Research (FCCCER) of the Department of Health and Human Services should it receive a legal mandate to determine whether any currently reimbursed medical or surgical treatment should be allowed.

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Any day, while we are all distracted by the fire and smoke arising from the great debates on health care reform, that mandate could slip under the radar as an amendment or rider to a totally unrelated congressional bill, like the creation of the FCCCER included in the $787 billion Recovery Act of 2009.[8] The elderly, who are affected most by this disease, may then awake to find that they are mandated to enter a painful new era on a road paved by research studies such as these.

Such an outcome must be clear to Dr Weinstein who, in his editorial in the same issue of the *New England Journal of Medicine*,[9] clearly recognized that these studies will be used by the government for exactly this purpose. I wish to remind him that it is one thing to tell a patient whom you do not know that he or she cannot have vertebroplasty on the basis of studies, regardless of whether they are as flawed as these studies, and it is quite another thing entirely to be either the patient whose life is limited by pain or a caregiver. I wonder whether the authors of these research studies and Dr Weinstein would proudly refuse vertebroplasty for themselves or their mothers in such a situation. If so, then let them find comfort in their own medicine. I am certain that their mothers would have a different opinion.

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COMMENTARY

Response to "Randomized Vertebroplasty Trials: Bad News or Sham News?"

We appreciate the opportunity to respond to the thoughtful editorial regarding our studies investigating the efficacy and safety of vertebroplasty that were published recently in the *New England Journal of Medicine*.[1,2] The author of the editorial presents his personal anecdotal experience of successful outcomes of vertebroplasty as "evidence" that vertebroplasty is efficacious, while suggesting that our results, based on the most rigorous of study designs, the randomized placebo-controlled trial, are erroneous. We would point out that the findings in our 2 independent studies of statistically significant and clinically important improvement, both immediate and sustained, following the procedure are in keeping with his anecdotal experience and the results of previous studies. The magnitude of improvement in pain in the vertebroplasty-treated groups was similar in the 2 trials and consistent with improvements reported in previous uncontrolled and controlled augmentation trials, including the VERTOS and Fracture Reduction Efficacy (FREE) studies.[3,4]

In contrast to previous studies, our trials compared the experiences of those who received vertebroplasty with those who received a sham procedure with the added methodologic constraint that treatment allocation was blinded in both participants and the outcome assessors, thereby reducing the potential for bias in estimating the treatment effect. Both trials observed that subjects in the control groups improved following the procedure, with neither trial demonstrating a difference between the active and placebo groups in the magnitude of improvement in pain or functional status. It would appear that it is this observation that is most difficult for the author of the editorial and others to accept. As discussed in both of our articles, possible explanations for a discordance between the perceived results of clinical practice and the results of unblinded uncontrolled studies versus the findings from blinded placebo-controlled trials include the self-limited natural history of vertebral fractures, regression to the mean, and the placebo response. While we consider it unlikely that local anesthesia would have a sustained effect, investigators at 1 site have already undertaken new trials to further probe the relevance of local anesthesia in painful vertebral fractures.

The author casts doubt on the validity of our trials by questioning the vertebroplasty techniques used in our studies. We are not aware of any evidence to support his view that the cement volume in our trials was suboptimal. The investigators of 1 of the trials previously found no association between cement volume and patient outcomes following vertebroplasty.[5]

Although neither trial reached the prespecified sample sizes, both trials had more than adequate power to detect clinically important differences between groups with respect to their primary efficacy end points. The a priori target sample size for the Australian trial[1] was large because the trial was also designed to test other hypotheses regarding safety, including incident fracture rate, which would have required a larger sample size. The Investigational Vertebroplasty Efficacy and Safety Trial (INVEST) was initially powered to detect very small differences in outcome, far less than the minimally clinically relevant difference in pain and function. The investigators of both trials would have been thrilled to enroll more patients, but recruitment was hampered by the widespread acceptance and availability of the treatment in both trial settings. Recent estimates indicate that well over 150,000 augmentation procedures are done annually in the United States. Vertebroplasty has been publicly funded in Australia since