required to establish the overall effectiveness of their method both in the animal model and in human beings.

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Reply to the Editor:

Dr Scrofani and his colleagues in Milan are to be congratulated for carrying out these fluoroscopic studies of implanted radiopaque mitral annular markers in human subjects. Scrofani's letter alludes to the radiographic results in 20 patients who had a few, relatively large (3 mm) metallic markers inserted into a posterior mitral annuloplasty tube of autologous pericardium, which were published in 1991¹ and 1996.² The Institutional Review Board at Ospedale "L. Sacco" and these courageous investigators deserve credit for conducting the only human investigation that I am aware of which employed intracardiac radiopaque markers; it is notable that no adverse complications of the research study were noted. When we began our myocardial marker studies in human patients in the 1970s, we used only external or left ventricular mid-wall myocardial markers. Our more recent investigations of the mitral ventricular-valvular complex, which now include upward of 10 miniature gold markers inserted in the mitral leaflets per se in addition to the 8 annular markers, have all been performed in animal models, including the article concerning the mitral annular ring in sheep, which prompted Scrofani's letter.³

Both similarities and differences between the normal sheep and the human postmitral repair studies are noteworthy, including the timing and amplitude of annular motion. This Italian group attempted to reproduce in human beings the seminal pioneering work performed by Tsakiris and colleagues⁴⁻⁶ in dogs at the Mayo Clinic in the 1960s. Importantly, only single-plane fluoroscopy was used, as was the case in Tsakiris's experiments, which means that cardiac motion into and out of the plane of reference and other internal motion (translation and rotation) were not detectable. This implies that the observed motion could possibly have not been true internal cardiac deformation, but corrupted by artifact resulting from cardiac translation or rotation. The high speed,

simultaneous biplane cinefluoroscopic techniques that we use eliminate such ambiguity, because the true 3-dimensional coordinates of each marker are identified every 17 ms with respect to a fixed, external laboratory reference system, with an accuracy and reproducibility of less than 1 mm.

Scrofani and associates noted that fractional area change of the posterior mitral "hemisphere" during the cardiac cycle was small ($8.5\% \pm 6\%$) after a partial posterior pericardial annuloplasty; importantly, this is not dissimilar to the total mitral annular area change of $11\% \pm 2\%$ reported in our study in control sheep.³ On the other hand, we found no mitral area change after implantation of either a complete Duran ring (Medtronic, Inc, Minneapolis, Minn) or a Carpentier-Edwards Physio complete annuloplasty ring (Baxter Healthcare Corp, Irvine, Calif).³ Given the marked differences in annuloplasty methods employed, analytical techniques used, the experimental conditions, and the species, there is little point in debating which measurement is more correct than the other. Much more noteworthy is that the Italian investigators observed a much smaller magnitude of dynamic motion of the human annular orifice after mitral repair than did the Japanese team of Okada and associates,⁷ who used extrapolated 2-dimensional echocardiographic imaging to make their measurements. Okada's group reported mitral fractional area reduction of $26\% \pm 4\%$ in patients who had received a Duran flexible annuloplasty ring,⁷ which was similar to that reported echocardiographically in normal human beings by Ormiston and coworkers⁸ in 1981. Again, these echocardiographic methods cannot differentiate true internal cardiac deformations from rotation and/or translation, cannot track the motion of discrete cardiac foci, and are limited in terms of temporal resolution, similar to the limitations inherent in contrast left ventriculography, nuclear multigated acquisition scanning, and magnetic resonance imaging (without radiofrequency tagging of discrete structural elements). Indeed, the advent of 3-dimensional echocardiography may even have complicated this issue more, as a recent abstract from the Cleveland Clinic Foundation reported mitral area changes of $25\% \pm 10\%$ in normal human beings and $28\% \pm 11\%$ in those who had received a Cosgrove-Edwards annuloplasty band (Baxter Healthcare Corp, Irvine, Calif) during mitral repair.⁹ These large fractional mitral area changes were associated with calculated end-diastolic mitral annular areas of $10.1 \pm 3.9 \text{ cm}^2$ in normal subjects and $11.5 \pm 2.7 \text{ cm}^2$ in patients who had an annuloplasty, clearly much larger than one would expect. Indeed, the normal mitral area is only 4 to 6 cm^2 as calculated from the Gorlin formula and, pathologically, measures only 6 to 8 cm^2 ; therefore, these 3-dimensional echo estimates of mitral area actually are supraphysiologic. This leads one to question what the 3-dimensional echo techniques are actually measuring. We all have been dazzled by beautiful 3-dimensional echo images of mitral valve leaflets opening and closing and wire-frame reconstructions of other cardiac structures, but it must be remembered that quantitative 3-dimensional echo measurements of discrete cardiac dimensions and dynamics have not yet been validated. Comparison of 3-dimensional marker data obtained from simultaneous

biplane high-speed cinefluoroscopy of implanted mitral annular radiopaque markers with 3-dimensional echo data would constitute the ideal validation benchmark, but such investigations have not been carried out to date, either in animals or in man. To this end, our laboratory, with the necessary video processing and coupled computer systems, would be pleased to collaborate with any serious investigator who has the capability to insert multiple miniature markers in the mitral annulus in patients and obtain high-quality biplane cinefluoroscopic images postoperatively.

Until that day arrives, the quest for the Holy Grail concerning human mitral valve pathophysiology will remain unfulfilled; furthermore, in my opinion, until more quantitative, validated 3-dimensional data are available, all 3-dimensional echocardiographic estimates of mitral valve area and fractional area reduction should be interpreted cautiously, because they may represent gross overestimates and reflect the motion of structures other than the mitral annulus per se.

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A word of caution in extrapolating the riluzole spinal cord injury protective effects obtained in a rabbit model under ketamine anesthesia

To the Editor:

We read with great interest the excellent article titled "Riluzole Prevents Ischemic Spinal Cord Injury Caused by Aortic Crossclamping" by Lang-Lazdunski and associates (*J Thorac Cardiovasc Surg* 1999;117:881-9). We do not doubt the protective effects exhibited by riluzole, and we believe this article is a significant contribution to central nervous system protection, for which the authors are to be congratulated. However, we would like to reiterate a point that was raised recently concerning an article on memantine.^{1,2}

The authors' anesthetic included 50 mg/kg of ketamine. Ketamine is an *N*-methyl-D-aspartate antagonist and known to confer significant protection of the central nervous system against ischemia.^{3,4} Since the mechanisms of action of ketamine and riluzole seem to be different, the likelihood of effects being even potentiating and not only additive are real. Thus the observed protective effects of riluzole were the result of the effects of riluzole by itself in addition to those contributed by ketamine, but their relative roles are unknown. For definitive assessment of the protective effects of riluzole alone, a group of rabbits anesthetized with nonprotective concentrations of volatile agents only, without ketamine or barbiturates, is essential before the data, concerning particularly the ischemic time, can be extrapolated to human application since ketamine is not usually used in adult human clinical practice.

We⁵ have found, in a similar model but without using ketamine, that neurologic functional recovery objectively evaluated 6 hours after reperfusion accurately reflects the subsequent outcome at 24 hours. We wonder whether the authors made neurologic score evaluations early after reperfusion and whether neurologic functional improvement was noticed between 24 hours and 120 hours in those observed for more than 24 hours.

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