

Interventional Rounds

Interventional Cardiology Live Case Presentations: Regulatory Considerations

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Live case presentations are increasingly common at interventional cardiology conferences. Taking advantage of significant advances in communication technology, broadcasts of procedures can be viewed as an extension of traditional medical education targeted to large groups of practitioners. However, there are important ethical, commercial, and patient safety issues associated with live cases that deserve attention. Use of investigational devices in live case demonstrations is subject to review and approval by FDA's Center for Devices and Radiological Health (CDRH), and the outcomes of patients participating in live cases are considered in the overall clinical study results. This article discusses CDRH's regulatory view of live case presentations with a focus on patient safety, clinical trial integrity, and concerns regarding improper medical device promotion. © 2010 Wiley-Liss, Inc.

Key words: complications adult cath/intervention; angiography; coronary; percutaneous coronary intervention

INTRODUCTION

The past two decades have witnessed a proliferation of live case demonstrations of interventional cardiology procedures to treat coronary artery disease, structural heart disease, peripheral vascular disease, and cardiac arrhythmias. These presentations have often become integral parts of the scientific sessions sponsored by cardiovascular professional societies, large research foundations, and some individual medical institutions.

Multiple ethical, promotional, and educational issues surround the issue of live case presentations. Sade et al., on behalf of the American Association for Thoracic Surgery Ethics Committee and the Society of Thoracic Surgeons Standards and Ethics Committee strongly question the value of live case demonstrations [1]. The authors highlight patient safety risks and questionable medical ethics associated with live cases. Although they recognize that the teaching of surgical techniques by direct observation of live surgery in the surgeon's home operating room is a time-honored acceptable practice, they conclude that the educational benefits of broadcast live cases are "meager" compared to the potential harms faced by the participating patient. Thus, they recommend that national and international cardiothoracic societies consider prohibiting live surgery broadcasts at their annual meetings.

In contrast, a writing group composed on behalf of several US and international cardiovascular professional societies, in the current issue of the *Catheterization and Cardiovascular Interventions*, the *HeartRhythm Journal* and the *Journal of the American College of Cardiology*, provide greater emphasis on the merits of live case demonstrations and view them as an evolutionary advance in physician teaching methods [2]. The authors attest to the inherent (but difficult to measure)

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Conflict of interest: This work represents the professional opinion of the authors and is not an official document, agency guidance or policy of the U.S. Government, the Department of Health and Human Services, or the Food and Drug Administration, nor should any official endorsement be inferred.

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Received 24 June 2010; Revision accepted 28 June 2010

DOI 10.1002/ccd.22718

Published online 21 September 2010 in Wiley Online Library (wileyonlinelibrary.com)

benefits of live cases for physician education, improved quality of medical care, increased enrollment in clinical trials, and fostering innovations in medical device development. Importantly, the writing group recognizes that there are no objective measures of the educational value derived from the observation of live cases, and there is a paucity of data on the potential safety risks to patients who are subjects of live cases. The authors rightfully acknowledge the critique of live case demonstrations presented by Sade et al.; in response, they offer a detailed program of measures aimed at mitigating patient risks and ethical concerns. Their suggestions provide mechanisms to standardize the performance of live cases to enhance patient safety and improve their educational value.

FDA's Role

FDA's broad public health mission is to provide assurance that drugs and devices are safe and effective for their intended uses. At FDA, the Center for Devices and Radiological Health (CDRH) is responsible for establishing reasonable assurance of the safety and effectiveness of medical devices prior to marketing in the United States. Within CDRH, the Office of Device Evaluation's Division of Cardiovascular Devices evaluates the safety and effectiveness of devices used in interventional and electrophysiologic cardiovascular procedures. The agency appreciates the range of opinions offered by the authors representing thoracic surgery and cardiology professional societies regarding the merits of live case demonstrations [1,2]. Although there are clear individual patient welfare and public health implications associated with live cases, it is important to appreciate FDA's oversight role and the scope of its regulatory review of these procedures.

Use of Investigational Devices in Live Case Demonstrations

FDA's most important role in the regulation of live cases occurs in the use of investigational non-FDA approved devices in patients enrolled in clinical trials in the US. It must be understood that the study of significant risk unapproved medical devices in any clinical study may only occur if a sponsor obtains approval of an Investigational Device Exemption (IDE, 21 CFR 812) from the FDA. An IDE allows the use of investigational devices in clinical trials of human subjects. Often, the objective of the clinical trial is to collect data on device safety and effectiveness to support a premarket approval application (PMA) or a premarket notification [510 (k)], which following FDA approval (PMA) or clearance [510 (k)], allows commercial marketing and use of the device. In other situations, an IDE is required if a sponsor is seeking a new indication for an approved device or the

clinical research study involves off-label use of an approved device. An IDE provides protection to human subjects and ensures monitoring of the clinical study.

In the context of an unapproved device being used in an IDE study, FDA defines a live case presentation as:

"Treatment of a human subject under the auspices of an approved or conditionally approved IDE, conducted and broadcast in real time, or recorded and broadcast at a later time, to an audience at a widely attended professional scientific meeting."

Since investigational devices are not available for use outside of an IDE study (and might not ever become available in the US if the device does not ultimately receive FDA approval or clearance), the Agency's view is that the use of an unapproved device in live case demonstrations should be limited to providing increased awareness of the IDE study for potential investigators and practicing physicians to augment the recruitment of study subjects.

FDA approval of a live case presentation under the auspices of an IDE study requires a formal request from the sponsor and a detailed review by FDA staff; the application should be submitted at least 30 days prior to the live case demonstration to allow adequate time for a comprehensive evaluation. The application form for a live case demonstration requires that the sponsor address many of the concerns presented by the professional organizations [1,2]. The sponsor should identify whether the case will be presented live in real time or videotaped for later broadcast. FDA's primary focus regarding live cases is patient safety, and specific patient protection measures include:

- Institutional Review Board (IRB) approval. Approval of the live case presentation by an independent IRB is required.
- Risk analysis. A justification for a real time broadcast should include a rationale describing why a videotaped presentation would not serve as an adequate substitute. Procedural risks that may be increased by a live case setting include infections, prolonged procedure and anesthesia time, increased radiation exposure, increased intravenous contrast use, distraction of the operator, and patient privacy concerns. The application should discuss measures to minimize these risks. Although a case videotaped for later broadcast might be associated with reduced risk compared to a live case, the application process for FDA review and approval for a planned videotape is the same as that for a case to be shown live.
- Informed consent. A signed informed consent that details potential additional risks posed by the live presentation must be obtained prior to subject participation. The consent document should outline

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confidentiality issues (e.g., broadcast of the procedure and possible recording for future viewing). A patient who agrees to be a subject in a live case should be informed that he or she should have no expectation of direct benefit as a result of his or her participation.

Live case demonstrations of investigational devices may be performed only at approved investigational sites by investigators who are currently participating in the study. Adherence to the study protocol, data collection, and reporting of adverse events apply equally to live cases as they do for all other patients enrolled in the IDE study. Any planned deviations from the approved IDE study protocol should be described and justified. Operators performing live cases must keep patient safety paramount and not compromise clinical decision-making or care for the sake of demonstrating a new device or technique. To reduce risks, we recommend that an on-site investigator (rather than the operator who is actively performing the procedure) primarily interacts with the off-site moderator and panel. Unanticipated adverse effects that occur during a live case presentation, or adverse effects that occur at increased frequency, should be separately reported to the FDA in an IDE supplement within 10 days.

Patients who participate in a live case count toward the total approved enrollment in the clinical trial, and procedural and clinical outcomes in these patients have the potential to affect the overall results of the study. Further, it is understood that live case patients may be chosen for specific anatomic or clinical features of interest (introducing selection bias), and their participation may violate study randomization or blinding. In the analysis of the study results, clinical outcomes of live case subjects should be analyzed separately and compared with the outcomes for the rest of the study population to assess whether these subjects were exposed to additional risks.

FDA is sensitive to any overt or implied commercial promotion of the investigational devices demonstrated in live cases. Sponsors should provide a rationale for why the live case presentation is not a form of product promotion or advertising, and unapproved devices should be clearly identified as investigational during the broadcast and discussion of the case.

Extremely high risk procedures or interventions in highly complex patients or anatomies are generally not suitable for live case presentation involving devices under IDE investigation. In addition, invasive procedures in children may be more technically challenging than in adults, and a live case presentation involving pediatric subjects must present no more than minimal additional risks. Live case demonstrations in pediatric patients are associated with special safety

concerns (technically challenging anatomic features and heightened attention to radiation exposure and blood loss) and patient protection considerations (including assent by the child and parental permission); the sponsor must comprehensively address these pediatric-specific concerns in the request to FDA for live case approval. Finally, use of an investigational device for compassionate use or in a continued access study (that is initiated after IDE enrollment has been completed) is not appropriate for live case presentations.

Use of FDA-Approved Devices in Live Case Demonstrations

When not part of an IDE study, medical devices may be used either (1) in accordance with their FDA-approved indications for use (on-label use), or (2) off-label. Off-label use refers to use of an approved medical product in diagnosis or treatments other than those explicitly included in labeling. Although off-label use of a medical product should not be interpreted as inappropriate or substandard clinical practice, in many cases, it does mean that data from well-designed clinical trials have not been developed that establish a reasonable assurance of safety and effectiveness for FDA approval for the specific condition. The on-label or off-label use of an approved medical device used in a live case demonstration is subject to IRB approval and informed consent. However, use of a device beyond its labeled indication should be publicly disclosed during the presentation. Although the planned use of approved devices that are not part of an IDE study in live cases is not subjected to FDA review and approval, the agency maintains an active interest in all live cases and can initiate disciplinary action if the live case encourages or commercially promotes off-label use of a medical device.

FDA's Reach

With advances in communication technology, interventional cardiology live case demonstrations are increasingly global in nature and are transmitted from medical centers worldwide. However, the FDA only has regulatory authority over live case presentations of investigational medical devices that are broadcast from sites within the US. It is our hope that high standards of patient safety, privacy, and ethics are also applied to live case procedures performed outside the US.

Summary

Live case presentations may be viewed as an extension of traditional methods of medical education in

an era of unparalleled growth of communication and broadcast transmission technology. However, the objective educational benefits of live case presentations are difficult to measure, and potential patient safety and ethical concerns need to be recognized. As a public health regulatory agency, FDA has important oversight of many aspects of live case demonstrations with patient protection as its highest priority. FDA is considering developing further guidance on live case presentations during IDE clinical trials. Lastly, as there have been few studies of adverse events or outcomes related to live cases [3,4], more research on procedural safety outcomes during live case presentations is needed to better define patient risks, particularly at a time in which live case presentations have become a cornerstone of many interventional cardiology meetings.

REFERENCES

1. Sade RM, American Association for Thoracic Surgery Ethics Committee and the Society of Thoracic Surgeons Standards and Ethics Committee. Broadcast of surgical procedures as a teaching instrument in cardiothoracic surgery. *Ann Thorac Surg* 2008;86:357–361.
2. Dehmer GJ, Douglas JS, Abizaid A, Berg JW, Day J, Hall R, Leon MB, Hijazi ZM, Marchlinski F, Park S-J, Popma JJ, Society for Cardiovascular Angiography and Interventions, American College of Cardiology/Heart Rhythm Society, European Society of Cardiology, Sociedad Latinoamericana de Cardiología Intervencionista, and Asian Pacific Society of Interventional Cardiology. Statement on the use of live case demonstrations at cardiology meetings: Assessments of the past and standards for the future. *Cathet Cardiovasc Interv* 2010; DOI 10.1002/ccd.22719.
3. Wood S. Show and tell or just plain show? Experts ponder the risks and benefits of live case demonstrations. Available at: <http://www.theheart.org/article/309435.do>. 06 November 2003.
4. Franke J, Reimers B, Scarpa M, Span S, Thieme M, Wunderlich N, Scheinert D, Sievert H. Complications of carotid stenting during live transmissions. *J Am Coll Cardiol Interv* 2009;2:887–891.