

**USE OF CONTRAST AGENTS IN CONJUNCTION WITH CARDIAC IMAGING
PROCEDURES IN THE PEDIATRIC POPULATION**

**Statement to the Advisory Committee Food and Drug Administration
From the Pediatric Council of the American Society of Echocardiography**

Good Afternoon Members of the Advisory Committee,

My name is Jack Rychik and I am a pediatric cardiologist with specialty interest in pediatric echocardiography. I am a staff member at the Children's Hospital of Philadelphia and I served as Director of Echocardiography at that institution from 1996 to 2003. Currently I am the Director of the Fetal Heart Program at The Children's Hospital of Philadelphia. I come before this Committee as a representative of the American Society of Echocardiography and as Chair of the Pediatric Council of the American Society of Echocardiography, or ASE.

The American Society of Echocardiography is an organization of nearly 9,000 professionals committed to excellence in cardiovascular ultrasound and its application to patient care through education, advocacy, research, innovation and service to our members and the public at large. As a member of this organization, and a physician with a strong interest in the clinical application of non-invasive imaging modalities in children, I am here to advocate for the promotion of the safe and effective use of ultrasonic contrast agents for cardiovascular imaging in children.

Ultrasonic imaging of the cardiovascular system, or echocardiography, is the most commonly used modality for imaging of the cardiovascular system in infants and children. The application of echocardiography in children (1) has an over 30 year track record of safety, (2) is an imaging modality which is highly reproducible with excellent temporal and spatial resolution, (3) provides for real time data on both cardiac structure and function, (4) and is a mobile technology, which means it can be performed repeatedly and serially at the patient bedside. As such, echocardiography has become the first line modality for imaging in children with cardiovascular disease and has grown tremendously in its use.

Despite its first line use, there are still some limitations of echocardiography, primarily related to difficulties in ability to acquire a complete and satisfactory image. Ultrasound is dissipated within tissue as it travels through long distances and is impaired by bony structures and air. These issues become of primary importance in older (larger) patients, however often-times acoustic windows, even in small children, can be poor which can lead to poor image resolution. The usual sharp distinction between the borders of blood and tissue can be blurred, thereby making it difficult to reliably measure cavity volumes and wall thicknesses, and consequentially impairing our ability to measure ventricular ejection and wall motion abnormalities.

Hence for our adult cardiology colleagues, the advent of echo-contrast agents has been extremely helpful. Intravenous injection of ultrasound contrast agents has been

documented to improve endocardial border delineation. Contrast enhancement of the blood tissue boundary has improved assessment of ventricular wall motion, wall thickness, calculation of ejection fraction and delineation of structural abnormalities. Recent experimental results indicate that echo contrast has the potential to provide qualitative and quantitative assessment of myocardial perfusion and coronary blood flow. This would add tremendously to the diagnostic capabilities of echocardiography. As we have heard, the safety profile of echo contrast agents in adults has been well defined, and there is currently a 3rd generation product approved for use.

Members of the advisory committee, the time has come for children to reap the benefits of this form of cardiovascular imaging. At present there is very little experience in the use of echo contrast agents in children, primarily since the safety profile in infants and children has yet to be well defined. However, there is great potential for the use of a safe echo contrast agent in a variety of conditions in children.

Some examples include:

- For use in delineation of endocardial border for volume, ejection fraction, and myocardial wall motion
- For use in evaluation of intra-cardiac shunts such as across a patent foramen ovale in the evaluation of a child with stroke
- For visualization of complex baffles and channels as part of repair of congenital heart disease, such as in the Mustard or Senning operation for transposition of the great arteries, or in the Fontan operation for single ventricle
- For use in improved visualization of thrombus in venous pathways of patients after Fontan operation for single ventricle (visualization of thrombus by conventional surface imaging is oftentimes a difficult task due to scatter created by the synthetic patch material used – contrast agents may be extremely helpful in reliably identifying thrombus and avoiding the need for further testing such as transesophageal echocardiography)
- For use in assessment of coronary artery flow and myocardial perfusion. Although coronary atherosclerotic disease in infants and children is rare, there is still a great need to reliably assess coronary flow in conditions such as:
 - Congenital coronary anomalies (before and after surgery)
 - Kawasaki Disease
 - After arterial switch operation for transposition of the great arteries
 - After Ross operation, in which coronary re-implantation is performed
 - After palliation for hypoplastic left heart syndrome, in which aortic reconstruction is undertaken and coronary flow potentially impaired

From personal experience, I would conservatively estimate that 5-10% of patients coming through our echocardiography laboratory at The Children's Hospital of Philadelphia are potential candidates who could benefit from the addition of contrast echocardiography to their examination. At our single center where close to 15,000 echocardiograms are

performed each year, this means that approximately 1,000 patients per year could potentially obtain incremental benefit from the use of this modality.

Members of the advisory committee, the American Society of Echocardiography has in the past taken the lead in providing a synthesis of available evidence justifying the adoption of relevant new technologies in the field of echocardiography as they develop. In addition, the ASE has played a key role in establishing guidelines for training and experience in the various modalities and uses of echocardiography. An ASE position paper on contrast echocardiography was released and published in 2000 (Mulvagh SL, DeMaria AN, Feinstein SB, et al. Contrast echocardiography: current and future applications. *J Am Soc Echocardiogr* 2000;13:331-42) and an update is currently planned for this year 2004. The ASE therefore plans to take an active role in the process of promoting the safe use of contrast echocardiography in children.

With growing interest in the subject, we have formed an Ad Hoc Committee of the Pediatric Council of ASE to look at the issue of “safety and utility of contrast echocardiography in children.” This committee is comprised of experts in pediatric echocardiography as well as adult echocardiography, professionals who can share their knowledge and experience in the use of contrast agents. It is the desire of this Ad Hoc committee, the Pediatric Council of the ASE and the ASE as a whole to promote and advocate for the expansion of the safe and effective use of contrast echocardiography in children and to develop guidelines for use and training.

We look forward to working with the FDA and acting as a professional resource to them as they move forward in these endeavors.

Respectfully submitted,
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Jack Rychik, MD
Chair, Pediatric Council
American Society of Echocardiography

Associate Professor of Pediatrics
The Children’s Hospital of Philadelphia
University of Pennsylvania School of Medicine
Phone: 215.590.2192
Fax: 215.590.3788
Email: rychik@email.chop.edu