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"This imaging technology has revolutionized echocardiography by improving the quality of our exams and by extending the type of exams we can perform."

Dr. Karl Q. Schwarz,  
cardiologist and director  
of the Echocardiography  
Laboratory at the  
University of Rochester  
Medical Center

# BUSINESS OPPORTUNITY IN ULTRASOUND

## Ultrasound Tissue Harmonic Imaging

Research Corporation Technologies (RCT) offers nonexclusive licenses for a landmark ultrasound tissue harmonic imaging (THI) technology.

Work in the early 1990s by P. Ted Christopher, Ph.D., at the University of Rochester's Center for Biomedical Ultrasound in New York, led to a new mode of ultrasound imaging that has become an important part of medicine today. This breakthrough, called tissue harmonics, enabled development of second- and higher-order harmonic responses of tissue to an ultrasound beam that produces a sharper image than that of the fundamental frequency.

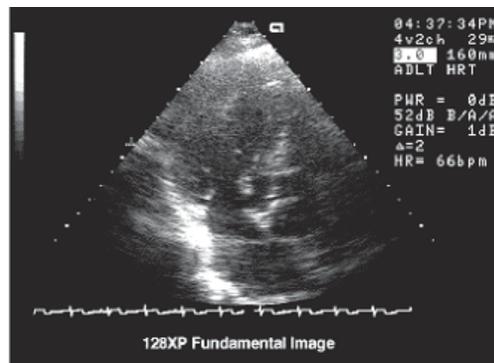
U.S. Patent No. 7,104,956 issued Sept. 12, 2006, with broad method and system claims to protect Christopher's seminal tissue harmonics discovery. The new patent complements U.S. Patent No. 7,004,905, which also has broad claims to protect Christopher's discovery, and U.S. Patent No. 6,206,833, which covers other aspects of the technology. Two other U.S. patents are pending.

### THE TECHNOLOGY

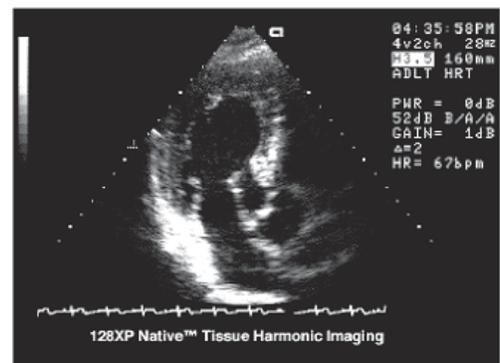
THI, tissue imaging at the second or higher harmonic frequencies, is a major advance in ultrasound that reduces artifacts and enables physicians to make better diagnoses.

Tissue harmonics originate naturally from the tissue itself as acoustical energy propagates through it. As an ultrasound wave travels through tissue, slight nonlinearities in sound propagation gradually deform the shape of the wave and generate harmonic frequencies. Use of these harmonics in tissue imaging improves spatial resolution, allowing visualization of smaller objects, and improves the contrast between subtle grayscale differences.

THI has been adopted rapidly by the ultrasound industry and is now available in a variety of technical implementations.



**Figure 1.** An ultrasonic image of an adult heart at the fundamental frequency.



**Figure 2.** Same ultrasonic image using Tissue Harmonic Imaging.



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**"Tissue harmonic imaging significantly improves visualization of both normal and pathologic tissues and its selective use has major diagnostic utility in a wide variety of clinical applications."**

Stanton J. Rosenthal,  
Paul H. Jones and Louis  
H. Wetzel, Phase Inversion  
Tissue Harmonic  
Sonographic Imaging:  
A Clinical Utility Study,  
*American Journal of  
Roentgenology*, June  
2001

## BACKGROUND

Early investigations using harmonic contrast agents led Christopher in the early 1990s to consider the physics of nonlinear propagation of ultrasound in tissue without contrast. This work led to the important discovery of THI, which exploits harmonic frequencies that are generated as a fundamental ultrasound wave propagates through tissue.

After several years of research and theoretical modeling, Christopher discovered that on a 2MHz machine, the 4MHz-and 6MHz-signals generated by distortion inside tissue could be read by a scanner and processed to produce images. The images gave a much clearer ultrasonic picture of the inside of the human body than images obtained using the fundamental ultrasound frequency.

Christopher's nonlinear model of ultrasound propagation in tissue operated in the frequency domain, but used spatial Fourier transforms to calculate diffraction effects. Removing restrictions on the position of the field points allowed him to estimate in-situ ultrasound exposure and model formation of ultrasound harmonic images.

From his model and subsequent experiments, Christopher showed THI enables better rejection of clutter noise than imaging using the fundamental component because the main lobe of a harmonic beam is narrower than that of the fundamental frequency beam. He found this characteristic results in reduced on-axis clutter and better suppression of near-field clutter.

## TODAY

The rapidly expanding body of scientific and clinical literature demonstrates the clinical usefulness of THI. Offering considerably better spatial resolution and reduced artifacts, THI provides maximum diagnostic information.

Use of THI has gained broad acceptance by ultrasound manufacturers and the clinical community. Reports emphasize the value of tissue harmonic imaging in obstetrics, abdominal and cardiology imaging. A patient's physical condition is no longer an obstacle to image quality and reliability. THI actually improves imaging in postoperative studies, as well as while scanning obese or otherwise technically difficult patients.

Since THI requires no use of contrast agents, this technique can be easily applied in daily practice without additional equipment, effort or cost. RCT believes THI supersedes all conventional Brightness Mode (B-mode) ultrasound imaging in most clinical applications.

## ADVANTAGES OF THI

- Improved signal-to-noise and contrast-to-noise ratios
- Enhanced visualization of deep structures
- Improves basic ultrasound limitations – penetration vs. resolution
- Uses lower frequencies for transmission
- Relative auto-focusing – harmonics are generated in the center of the beam where acoustic pressure is maximal
- Contains minimal noise and clutter compared to fundamental imaging
- High-frequency imaging and one-way travel back to the transducer produces a superior image
- Reduced reverberation, beam aberration, beam side lobes and haze
- Better lateral and axial resolution

### APPLICATIONS

- Obstetric imaging
- Abdominal imaging
- Cardiac imaging
- Breast imaging



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**"Tissue harmonic  
imaging has already  
earned a role as an  
indispensable,  
commonly used  
US mode."**

*RadioGraphics*  
July - August 2003

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## PATENTS

U.S. Patent No. 7,104,956, "Finite amplitude distortion-based inhomogeneous pulse echo ultrasonic imaging," issued Sept. 12, 2006

U.S. Patent No. 7,004,905, "Finite amplitude distortion-based inhomogeneous pulse echo ultrasonic imaging," issued Feb. 28, 2006 (continuation of application U.S. Ser. No. 08/746,360, filed Nov. 8, 1996)

U.S. Patent No. 6,206,833, "Finite amplitude distortion-based Inhomogeneous pulse echo ultrasonic imaging," issued March 27, 2001

Two other U.S. patents are pending.

## ABOUT RCT

RCT manages the THI technology for its partner, the University of Rochester in New York. Acuson Corporation - a Siemens company, Royal Philips Electronics, General Electric, Biosound Esaote and Toshiba are licensees of the THI technology. RCT continues its efforts to license the technology broadly to the ultrasound industry. All licensing agreement terms are confidential. RCT is instrumental in the commercial successes of many important technologies including the anticancer agents cisplatin and carboplatin, the PSA blood test for prostate cancer, the *Pichia* Yeast Protein Expression System and the Blue Noise Mask halftoning technology.

## RECOMMENDED READING

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Mike Averkiou, "Tissue Harmonic Ultrasound Imaging," *C.R. Acad. Science Paris*, t. 2, Series IV, p. 1139-1151, (2001)

Terry S. Desser and R. Brooke Jeffrey, "Tissue Harmonic Imaging Techniques: Physical Principles and Clinical Applications," *Seminars in Ultrasound, CT, and MRI*, Vol. 22, No. 1, p. 1-10, (Feb. 2001)