Revitalized old technology spurs new interest, applications

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Although the roots of traditional geometric x-ray tomography date back to the 1930s, the technique was not practical at that time because image receptors could not provide large-area dynamic scanning. The technique, renamed tomosynthesis in the 1970s, acquired only one imaging section at a time, requiring additional time and radiation dose to obtain more imaging sections. It's not hard to understand why, therefore, plain-film tomosynthesis fell by the wayside as soon as CT came along.

"Everyone was happy to give up plain-film tomosynthesis because it was cumbersome to get multiple films, and it had high radiation exposure," said Dr. H. Page McAdams, a professor of radiology at Duke University Medical Center in Durham, North Carolina.

It wasn't until the late 1990s, with the advent of flat-panel digital detectors, that investigators began to realize that perhaps tomosynthesis was viable after all.

Digital tomosynthesis systems gather a series of projection images as an x-ray tube moves along a prescribed path in a single motion. The systems then retrospectively reconstruct the images in multiple sections or in-focus planes to produce a 3D volume. The result is a quick and inexpensive way of gaining volumetric scans without high doses of radiation.

"Now the technique allows you to get section images with an exposure that is essentially equivalent to a lateral chest radiograph in a very short period of time. So an older technique is being revitalized by new technology. A new era for tomosynthesis is just beginning," McAdams said.

THE EARLY DAYS

Tomosynthesis initially focused on vascular, dental, and chest imaging, and it was crude and technically limited in its first incarnation. The technique relied on conventional fluoroscopy image intensifiers and equipped them with a digital camera to acquire and later reconstruct digital images. Images from image intensifiers have significant barrel distortion, which is not a problem for fluoroscopy. Objects are squeezed along the periphery of the visual field, and registration points are off by about 1 cm. Because this type of distortion is uniform, it doesn't affect the perception of a fluoroscopic image. But 1 cm of misregistration in an arc of multiple views is disastrous. It totally wipes out the resolution, said Dr. Michael J. Flynn, a physicist with the Henry Ford Hospital System in Detroit, Michigan. Software packages, such as Dyna CT from Siemens Medical Solutions and Xper CT from Philips Medical Systems, attempted to bridge the gap by reconstructing tomo images from fluoro systems.

Tomosynthesis is coming to market now because of the performance characteristics of modern flat-panel digital radiography. The most important attribute of flat-panel technology is the lack of distortion.

"The flat-panel surface is laid out in specific rows and columns, and you know exactly the geometry that the image has been recorded on. So you can do back projections for reconstructions and come back to the precise point in the tomographic layer that the data came from," Flynn said.

Digital detectors also are efficient. They detect nearly all of the x-rays that are coming in, which keeps the radiation dose low in relation to noise, he said.

Initial tomosynthesis systems nevertheless were still not fast enough. Breast tomosynthesis prototypes that were being tested in the 1990s were limited by the number of frames that could be read per second. The objective is to acquire at least 30 images in an arc within a few seconds, Flynn said, but some of the first experimental breast tomosynthesis devices could run only about four frames per second.

The current generation of systems can read out at 15 or 30 frames per second, making it possible to acquire the necessary number of images in an arc in a reasonable length of time. The experimental
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DEBLURRING AND PRACTICAL ISSUES

Tomosynthesis images can still be plagued by blur, however. Whenever a tomosynthesis image is captured in the traditional way, images in the focal plane are in sharp focus, but there is residual blur from structures residing above and below that plane.

"When you get a tomosynthesis image in the very vanilla way that's been around for decades, which is called shift and add, you need to do some type of deblurring to remove those blurry artifacts for high-quality imaging," said Dr. James Dobbins, an associate professor of radiology and biomedical engineering at Duke.

Several algorithms have been developed to remove blurring. Matrix inversion tomosynthesis technique, which is used at Duke, applies linear algebra to unwrap the known imaging geometry in tomosynthesis and to pull the blur components out of the slices from a finite number of planes.

Filtered back projection varies the filter kernel depending on the projection angle, and maximum-likelihood expectation maximization repeatedly adjusts 3D images and predicts 2D images as if the anatomic target really matched the 3D image.

High-quality tomosynthesis images depend on the manner in which they are obtained. Image acquisition needs to apply the characteristics of the tomosynthesis system to the characteristics of the body part that is being scanned, Flynn said. The detail in a tomosynthesis image tends to run in the direction of the acquisition, or the linear arc that a tomosynthesis system is following, and in the plane of reconstruction. Detail perpendicular to the acquired arc and the slice thickness is rather poor. Imagers need to think in terms of how the tomographic plane relates to the size and shape and orientation of the imaging target.

When scanning the proximal femur, for example, Flynn gathers three views that place the slice of the reconstruction at specific orientations relative to the head of the bone. One plane goes right through the head and neck of the femur and trochanter. This view can be captured by elevating the hip about 20 degrees, then taking the toe of the leg and pointing it in. That imaging position rolls the proximal femur over and makes the neck of the bone appear flat.

The second plane goes through the head and neck of the femur and trochanter at a 60 degrees rotation. This view is obtained by having the patient draw up the knee 60 degrees and rotate it outward about 30 degrees.

The third plane seeks transverse cuts through the neck of the femur.

"We can't quite get that view, but if we roll the unaffected hip up 60 degrees and then bring the knee out and lay it flat on the table, we can get an arc through the hip that is a modification of the classic orthopedic Lequesne, or false profile, view, which is reported in the literature for radiography," Flynn said.

Because tomosynthesis replaces a single conventional radiograph or a pair of anteroposterior and lateral views with a stack of images, it most likely will add to radiologists' per-case viewing time.

Dobbins doesn't think that time will be unduly burdensome because radiologists will be in a dynamic stack viewing mode.

"Radiologists will be able to scroll through the stack of images under user control at their PACS workstation and quickly decide whether any pathology is present or not. Then they can spend more time looking at the slices where there might be something," Dobbins said.

An early study of radiologists' experience with tomosynthesis in the chest indicates that abnormalities are fairly obvious, much more so than in conventional chest films.

"Tomosynthesis images have the same presentation as chest films, so they are familiar to radiologists. But they allow radiologists to see in much greater detail structures that otherwise could be completely invisible. So there's a great deal of enthusiasm about the ability of tomosynthesis to give a much better view of what is going on in the anatomy," Dobbins said.

USE IN CHEST IMAGING

Looking at the chest is a complex and challenging task because of the need to scan for a wide range of diseases within an anatomic area with overlying structures that compromise lesion conspicuity.

Soft-tissue structures in the lungs and blood vessels and the ribs all mask subtle anomalies such as lung tumors.

The motivation behind development of tomosynthesis for chest imaging is to improve the visibility of subtle lesions by generating slices through the lung, Dobbins said.

Tomosynthesis is doing just that, according to preliminary findings from a study of 130 human subjects and hundreds of CT-confirmed pulmonary nodules. The study, which is being funded by the
National Institutes of Health and conducted at Duke, found an almost twofold increase in the detectability of pulmonary nodules with tomosynthesis compared with standard AP radiography. Dobbins acknowledges that the ultimate clinical performance of tomosynthesis probably will not match the twofold degree of improvement found in this study, because radiologists had a CT scan in hand so they knew where to look for nodules in tomosynthesis scans versus x-ray films. Still, the results are highly encouraging. They show in particular that tomosynthesis is superior to chest films in visualizing lung nodules between 4 mm and 15 mm in size, McAdams said. Nodules greater than 15 mm are probably equally visible on plain films, although tomosynthesis has some advantage even with larger nodules in the presence of overlapping structures.

The sensitivity of tomosynthesis for finding nodules that are below 4 mm most likely will drop off significantly, however, because of diminished contrast resolution, McAdams said. Tomosynthesis therefore has a potential advantage over chest radiography for maximizing the sensitivity of the detection of nodules in the range of 4 mm to 15 mm but will not rival CT in detecting smaller lesions. If it turns out that population-based prospective screening for lung cancer becomes a reality, CT will be the gold standard for imaging the lungs because of its superior depth resolution. Tomosynthesis may nevertheless play a role because it has a relatively low radiation dose and is inexpensive.

"Tomosynthesis is not intended to be a replacement for CT in lung screening. Rather it is intended to be a vast improvement over chest radiography. And because many lung cancer cases are discovered at chest radiography, we're trying to develop a better front-end detection method for identifying lung cancer compared with regular chest radiography," Dobbins said. Tomosynthesis may replace CT as an intermediate problem-solving tool, however.

"Many times on routine chest film, we'll see something that looks like a nodule, but we're not really sure. It might be a vascular crossing or an osseous lesion. In years gone by, we would do chest fluoroscopy as opposed to CT. But with CT so readily available, most of those patients are going to CT to rule out a lung nodule. It's possible in that setting that tomosynthesis may be a low-cost, low-radiation-dose alternative to CT," McAdams said.

It also may be possible to turn to tomosynthesis to track nodule size over time, although the technique would not be as effective as CT for looking at the mediastinum or for looking at metastases in the rest of the body, McAdams said. It may also be used in place of chest radiography to scan for small nodules that could be metastases in patients with sarcoma.

A software component for GE Healthcare's Definium 8000 radiography system will generate high-resolution slice images of the chest as well as the abdomen, spine, and extremities. For imaging the chest, VolumeRAD makes a sweep of 30 to 60 varied low-dose images that can be rebuilt into approximately 40 slices similar to those obtained with CT except they are in the normal chest imaging plane, said Dave Widmann, GE's global marketing manager for general radiographic products and fluoroscopy.

VolumeRAD is considered an adjunct to conventional radiography. The Philips MultiDiagnost Eleva offers similar features.

"It is an investigational tool that will hopefully give better visibility to physicians on radiography so they can make a better second diagnosis or make a better informed decision about who goes on for CT," Widmann said

MUSCULOSKELETAL IMAGING

Tomosynthesis may emerge as the exam of choice relative to CT in musculoskeletal imaging, particularly of the knee and hip.

"The numbers are small, and we haven't done statistically significant controlled studies at this point, but we have a growing number of case results that compare 64-slice CT reformatted scanning and tomosynthesis done on the same day. The more we accumulate this case material, the more comfortable we become with the fact that tomosynthesis shows us pathology we just don't see on CT," Flynn said.

Although tomosynthesis repeatedly demonstrates about a threefold better in-plane resolution compared with CT, Flynn is careful to say that he doesn't think the technique is better than CT. It's just different.

"For problems where high detail can be of value, even given the fixed slice, we think tomosynthesis has a very definite role, and it perhaps may be the preferred method for getting a volumetric 3D assessment," he said.

Tomosynthesis is unrivaled in making the diagnosis of fractures of the subcondyle and cancellous bone that are suggested by a finding of bruising on MRI or clinical presentation but are otherwise occult, according to Dr. Marnix Van Holsbeeck, director of musculoskeletal radiology and emergency
radiology at Henry Ford Hospital.

Bone detail on MRI is fairly poor overall, and, although MRI is sensitive to edematous changes that accompany a fracture, blood can pool in areas that are far removed from the location of an actual fracture. Van Holsbeeck has found several fractures in patients with positive MRI findings that were in totally different spots on tomosynthesis images.

Fractures also have shown up on tomosynthesis that were not all that obvious on CT because the pixel-per-pixel resolution on tomosynthesis is superior, and as a radiographic technique, it is sensitive to bone calcium. Orthopedic surgeons at Henry Ford are coming to rely on tomosynthesis, especially when evaluating elderly or emergency patients who have a sudden change in gait or can't walk yet have normal x-rays. Orthopedists are making tomosynthesis the second-line examination after x-ray because it shows them pathologies in the same AP or lateral dimension they are used to, Van Holsbeeck said.

WEIGHT-BEARING VIEWS

Tomosynthesis can be done with the patient in a standing weight-bearing position, a plus for evaluating spontaneous osteonecrosis that may be confused with fracture. Orthopedists viewing bone on bone in a weight-bearing position can determine where cartilage has worn down and where bone conflict occurs, Van Holsbeeck said.

 Flynn and his colleagues at Henry Ford have been testing a tomosynthesis system, based on Shimadzu's Safire II selenium flat-panel detector technology, that can acquire 30 pulsed frames per second with precise geometric registration to a moving gantry. As many as 90 exposures can be acquired in one sweep, and large anatomic areas can be scanned with the 17-inch flat-panel detector. Tomosynthesis technology is incorporated in Shimadzu's radiography/fluoroscopy system, which facilitates weight-bearing scanning of the hips and knees and allows imaging of scoliosis in the spine.

The largest number of test cases for tomosynthesis at Henry Ford has involved the standing knee, followed by the proximal femur at the hip and the shoulder. Increasing numbers of investigations are being done of the wrist and foot, and a small number have looked at long-bone problems such as stress fractures or lytic lesions. The initial work was done with either a 9-inch or 12-inch field protocol. Flynn is now starting to develop 15-inch or 17-inch protocols for the spine.

Dr. Richard Prince of the University of Western Australia has been studying bone structure by means of volumetric x-ray absorptiometry (VXA), which falls under the umbrella of tomosynthesis. VXA is being developed by Hologic as a method for diagnosing osteoporosis.

"It's not only the amount of bone within bone, which is basically the definition of osteoporosis. We now also know from biomechanical considerations that size is important, and we are hopeful that this new procedure will give us a much better idea about bone size because it defines the edges of bone in 3D rather than 2D," Prince said.

The standard approach for evaluating osteoporosis-dual x-ray absorptiometry (DXA)-scans across a patient in an x/y direction and produces a picture as if the patient had been collapsed into two dimensions. VXA, in contrast, takes four images from four different angles and reconstructs a 3D volume similar to a CT, said Dr. Kevin Wilson, scientific director for Hologic.

While DXA measures the density of bone, which is a gross assessment of bone strength, VXA obtains macrogeometric properties of bone, such as the shape and density of the proximal femur, in order to measure in 3D such engineering parameters of the distribution of mass as the cross-sectional moment of inertia and the cross-sectional area.

Dr. Jeffrey Duryea, an assistant professor of radiology at Harvard University, believes tomosynthesis has the potential to measure changes in bone structure, such as narrowing of the joints in patients with osteoarthritis or erosions in individuals with rheumatoid arthritis, to quantify in 3D the degree to which arthritis is progressing.

"There aren't any structural modifying therapies with arthritis that may stop or reverse the disease. Essentially, the therapies now are just painkillers. But a great deal of effort is going on in developing potentially curative therapies, and once these treatments are on the market, there will be a need to assess patients on an individual basis to determine if a particular therapy is working or not. Tomosynthesis may provide an objective way of doing that," Duryea said.


His findings showed that the technique not only revealed joint margins and trabecular structure but also allowed measurement of joint space width. He is currently seeking funding to further explore tomosynthesis for arthritis imaging as a possible adjunct to mammography.
"Because we would be imaging small objects-knees and hands-tomosynthesis would tie in with mammography. The requirements for mammography are very high spatial resolution using relatively small detectors with a relatively low-power x-ray source. I would anticipate piggybacking on digital mammography or mammography tomosynthesis. You might be able to take a system that's designed for mammography and make some changes to the design to be able to scan knees and hands and feet as well," he said.

**USE IN BREAST IMAGING**

The purpose of tomosynthesis in imaging the breast is simple: to address the limitations of mammography. While mammography is the most efficacious method for detecting early breast cancer, it misses perhaps 20% of malignancies and performs poorly in younger women with dense breasts, who tend to have more rapidly growing cancers. Mammography suffers when imaging this population because normal fibroglandular tissue and tumors have similar x-ray attenuation, so they appear on a mammogram in exactly the same shade of white or gray.

"Mammography can end up hiding a pathology if a tumor happens to be situated among other normal breast tissue. Mammography also may produce a superimposition in which normal tissue mimics pathology on a 2D image that must be further investigated with additional imaging," said Dr. Andrew P. Smith, principal scientist for Hologic. "But if you can envision a 3D tomosynthesis image or thin slice through the breast, you would have little overlap of tissue above and below the pathology you're interested in. By looking at thin cross-sectional slices through the breast, you reduce the probability of having two pieces of normal tissue superimposing on one another to look like pathology, and you might reduce the callback rate."

Hologic is one of several imaging manufacturers actively developing tomosynthesis for breast imaging. The company is testing its prototype breast tomosynthesis unit at five clinical sites in the U.S. and one in Europe. It hopes to submit data from these studies to the U.S. Food and Drug Administration in the next few months and bring its unit to market within a year.

GE and Siemens have similar development timelines for their breast tomosynthesis systems, and a few smaller companies in Europe are just beginning to develop tomosynthesis products. Although details are still being worked out, it is likely that breast tomosynthesis will be incorporated in existing digital mammography products at least in the short term.

Over the long term, the technology faces wide opportunity. Tomosynthesis one day may completely replace mammography for breast cancer screening and diagnosis, and it may become the principal form of guiding breast intervention, according to manufacturers.

"We think tomosynthesis will really impact screening mammography, because we think it will dramatically decrease the recall rate and improve the cancer detection rate," Smith said. "It certainly has a role in diagnostic imaging because a 3D image is a natural way of problem solving when something is being obscured because other tissue is in the way. Tomosynthesis also has a role in interventional mammography because it gives the complete 3D coordinates of a pathology in an image and identifies where to take a sample of tissue."

One of the first investigators to test tomosynthesis in the breast, Dr. Joseph Lo, an assistant professor of radiology at Duke, is in the midst of a clinical trial of the technology that has enrolled 200 human subjects to date. Preliminary findings, which were presented at the 2006 meeting of the Radiological Society of North America, showed that tomosynthesis was more sensitive than mammography in lesion detection. In 144 patients, tomosynthesis detected 27 of 30 lesions for a 90% sensitivity rate, while mammography picked up 21 lesions for a sensitivity of 70%.

"There were all these lesions that were not seen on mammography except in retrospect. We went back carefully over old mammograms, and sure enough, there were lesions that had been there for years. We just had not seen them," Lo said.

The prospect of finding abnormalities that might otherwise have been dismissed or not seen at all suggests that tomosynthesis may increase the callback rate. But Lo found tomosynthesis had a callback rate of only 10% compared with mammography's rate of 15%.

"When you pancake tissue down into a 2D mammogram, tissues that overlap one another start looking suspicious. But if you spread it out in 3D, then you see one piece of tissue going one way in one plane and another going the other way in a different plane. And there's nothing suspicious about it at all," Lo said.

**A BRIGHT FUTURE**

Lo recalls that, in an impromptu panel discussion at the 2006 RSNA meeting, many of the luminaries of tomosynthesis development were surprisingly positive about the utility of the technique.
"You know, many things have been proposed in breast imaging over the decades, and some have taken on an adjunctive role to mammography. This one has the potential to replace mammography," Lo said. "Not right away, maybe, but eventually. When it comes to the whole package in terms of sensitivity, image resolution, cost, and speed, breast tomosynthesis is pretty much unique."

Karen Sandrick is a contributing editor for Diagnostic Imaging.
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