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Chest Tomosynthesis: Technical Principles and Clinical Update

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Abstract

Digital tomosynthesis is a radiographic technique that can produce an arbitrary number of section images of a patient from a single pass of the x-ray tube. It utilizes a conventional x-ray tube, a flat-panel detector, a computer-controlled tube mover, and special reconstruction algorithms to produce section images. While it does not have the depth resolution of computed tomography (CT), tomosynthesis provides some of the tomographic benefits of CT but at lower cost and radiation dose than CT. Compared to conventional chest radiography, chest tomosynthesis results in improved visibility of normal structures such as vessels, airway and spine. By reducing visual clutter from overlying normal anatomy, it also enhances detection of small lung nodules. This review article outlines the components of a tomosynthesis system, discusses results regarding improved lung nodule detection from the recent literature, and presents examples of nodule detection from a clinical trial in human subjects. Possible implementation strategies for use in clinical chest imaging are discussed.

Keywords

tomosynthesis; chest radiography; pulmonary nodules

Introduction

Digital tomosynthesis is a newly available imaging modality that offers the potential to be a substantial improvement over conventional chest radiography for the detection of subtle lung disease. It is a form of limited angle tomography that allows for the reconstruction of multiple section images from a set of projection images acquired as the x-ray tube moves along a prescribed path. Although originally conceived of many decades ago, tomosynthesis has only recently become practical for clinical use. Two commercial devices are currently on the market for chest imaging. Contemporary tomosynthesis devices use a conventional x-ray tube, a digital detector, a custom designed device to move the x-ray tube, and appropriate reconstruction algorithms. Tomosynthesis has recently been applied to chest imaging for the detection of subtle pulmonary nodules, with very promising results.

This review will present the basic principles of digital tomosynthesis and will summarize the most recent clinical evaluations of this technique in chest imaging. Although tomosynthesis

has potential utility in a variety of chest imaging applications, the one most commonly investigated is detection of small lung nodules, which will be the primary focus of this article. Other less investigated applications will also be briefly described.

Challenges in Chest Imaging

Chest radiography remains the mainstay for diagnosis of many lung diseases, despite advances in cross-sectional imaging techniques such as CT. It is frequently the first and may be the only imaging test performed in patients with known or suspected lung disease. It very likely remains the most commonly performed diagnostic imaging test worldwide (1). Over the past one hundred years, technological advances have resulted in many improvements in chest radiography. Advances in electronics and computer technology have led to the development of digital image receptors and displays (2). New image processing techniques, advanced applications such as energy and temporal subtraction radiography (3, 4), digital tomosynthesis (5-7), and computer-assisted detection and diagnosis (8, 9) promise to substantially improve on the performance of conventional chest radiography (1).

Of all diagnostic imaging studies, chest radiography presents some of the most difficult challenges. These challenges include, but are not limited to, issues related to image area and patient habitus, latitude and dynamic range of x-ray transmission through the chest, scattered radiation, overlap of anatomic structures, and limitations in perception of abnormalities (1). Further, numerous disease processes must be consistently depicted, including malignancy, infection, interstitial lung disease, airway disease, chest trauma and, in the intensive care unit, placement of support devices. Chest radiography is particularly challenging because the anatomy or pathology of interest is often quite subtle and can be quite difficult to perceive.

Detection of pulmonary nodules is certainly one of the most challenging tasks in chest imaging. Although nodules are very often seen retrospectively when reviewing previous images of patients with known lung nodules (10), identifying them prospectively is a difficult task. Even very experienced chest radiologists miss up to 30% of such lesions on conventional chest radiographs (11). Based solely on attenuation properties, nodules as small as 3 mm should be visible. However, in practice, reliable detection of nodules is often not possible until they are at least 8 mm in diameter. This limitation makes detection of smaller lesions, particularly small lung cancers, quite difficult.

The primary factor limiting detection of lung nodules and other similarly sized objects is their poor conspicuity in the presence of overlying anatomical structures such as lung vessels, heart, ribs, spine and clavicles ("anatomic noise") (12, 13). One method for improving conspicuity of small lung nodules is dual-energy subtraction imaging (3, 14-19). This technique quite effectively reduces visual distraction from overlying bone and can improve lung nodule detection. However, dual-energy imaging is limited in that it does not reduce visual clutter from overlying soft-tissue structures such as vessels.

A better method for improving nodule detection would be tomographic imaging, because it reduces the visual distraction from overlying structures of any tissue type. The current standard for lung nodule detection and characterization is computed tomography (CT), but it is expensive relative to conventional radiography and can impart a significant radiation dose to the patient (20, 21). While there are numerous strategies for reducing radiation dose from CT (22), CT remains an increasing source of population radiation exposure (20). Studies evaluating relatively low-dose CT methods for detection of lung nodules in lung cancer screening programs have confirmed a high sensitivity for small lung nodule detection (23-31). However, due to cost, workflow and radiation exposure issues, it is unlikely that CT will supplant conventional chest radiography in the near future for general thoracic imaging. Thus, a tomographic method that improves upon chest radiography, but without the cost or

radiation dose of CT, could be useful for enhancing the detection of pulmonary nodules in routine practice.

Digital Tomosynthesis

Digital tomosynthesis is an imaging technique that yields some of the tomographic benefits of CT but at reduced cost and dose (5, 6, 32). Although tomosynthesis has better spatial resolution in the x-y plane (i.e., coronal plane) than CT, it does not have as good a resolution in the depth direction. Despite this tradeoff, tomosynthesis still permits improved performance over conventional chest radiography. Tomosynthesis also has the advantage that it can be easily implemented as an adjunct to a conventional chest radiography exam.

Tomosynthesis is an improved version of the older technique of geometric tomography, which is now rarely performed in chest imaging due to positioning difficulties, high radiation dose, residual blur from out of plane structures, and competition from CT. Unlike geometric tomography, tomosynthesis is not limited to reconstruction of a single plane, but can generate an arbitrary number of slice images throughout the entire volume of the patient following a single low-dose acquisition of projection image data. Most of the current work with chest tomosynthesis uses images acquired in the conventional posteroanterior (PA) projection to reconstruct longitudinal section images (32, 33).

The technique for reconstructing longitudinal planes in a patient from a set of projection images has been around for many decades, going back to the work of Ziedses des Plantes (34), Garrison (35), Miller (36) and Grant (37). A variety of tomosynthesis implementations have been reported over the years, including work by Edholm (38), Ghosh Roy (39), Maravilla (40), Chakraborty (41), Webber (42, 43), Kolitsi (44), Wu (45), and our own laboratory (46-53). Clinical uses of tomosynthesis have included vascular imaging (54), dental imaging (55-59), orthopedic imaging (60, 61), mammographic imaging (7, 45, 51, 62-72) and chest imaging (5, 32, 33, 50, 52, 73-75). A review article published from our laboratory in 2003 describes in greater detail the history, mathematics, and reconstruction methodologies of tomosynthesis imaging (50).

Early investigation of tomosynthesis for chest imaging used digitized video output from an image intensifier. While this work demonstrated that tomosynthesis was feasible for chest imaging, it suffered from various drawbacks incumbent with image intensifiers. Several technological advances within the past ten years have now made tomosynthesis clinically practical. The most significant advance has been the development of flat-panel detectors. These detectors have high detective quantum efficiency, few artifacts, and are self-scanned at a rate suitable for rapid image acquisition needed for tomosynthesis. Other important technological developments that have facilitated recent tomosynthesis work include improved deblurring algorithms to suppress blur from out-of-plane objects (52, 76, 77) and increasing computer speed that enables reconstruction times suitable for clinical use.

Basics of Chest Tomosynthesis

Figure 1 depicts the standard components of a typical chest tomosynthesis system. The patient is positioned in front of a stationary flat-panel detector, and a motorized tube crane causes the x-ray tube to move in a vertical path. Images are acquired rapidly during the course of tube movement, and are read out in coordination with the x-ray generator. A workstation is used to reconstruct the tomosynthesis section images.

We constructed a prototype chest tomosynthesis system in our laboratory. It was used for studies designed to optimize image acquisition parameters (49, 52, 78, 79) and to collect human subject data for an NIH-funded clinical study (5). In order to illustrate the various

components in some detail, a description of this prototype unit will be given below. All of the tomosynthesis images presented in this article were acquired with this prototype system. Where appropriate, differences between this prototype and a commercially available tomosynthesis device will be highlighted.

Our prototype system uses a single-tile 41 cm × 41 cm amorphous-silicon flat-panel detector equivalent to one used in a commercial digital radiography product (Revolution™, GE Healthcare, Milwaukee, WI). The x-ray generator is capable of rapid, short exposure pulses and a 0.6 mm nominal focal spot is used. An x-ray anti-scatter grid is employed (Mitaya grid, 13:1 ratio, 78 lines/cm). The imaging geometry is the same as that of a traditional PA radiographic exam, with a 183 cm source-to-image distance.

The x-ray generator is coordinated with a custom-designed tube mover that moves the x-ray tube under computer control. Two linear actuators are used to move the tube vertically and rotate it about an axis so that it remains facing the center of the detector during its vertical motion. Our optimized acquisition procedure acquires 71 projection images over a total tube motion of 20 degrees (52). These projection images are acquired in 11 seconds, which is comfortably within a single breath-hold for most patients. In a commercially available tomosynthesis product (VolumeRad, GE Healthcare), a custom-designed tube crane is used that can move the tube for use with either a vertically-mounted wall stand or horizontal tabletop, and the commercial product acquires 61 projection images over a wider range of tube motion.

The first step in the reconstruction procedure is to perform a simple shift-and-add computation, equivalent to simple backprojection, to generate conventional tomosynthesis images. Figure 2 demonstrates how the shift-and-add method works. In the patient depicted in Figure 2A, there are two planes of interest, one containing a circular object and another containing a triangle. In the five projection images acquired in this simple example, the circle and triangle are projected onto different places in the imaging detector based on their relative height above the detector and the distance between tube locations. These five images can then be shifted in such a way that the circles all line up and the triangles are spread out in a manner reminiscent of image blur (Figure 2B); alternatively, the images may be shifted by a different amount so that the triangles line up and the circles are blurred out. By changing the amount of shift, a series of tomosynthesis slice images are generated throughout the entire volume of the patient. A spacing of 5 mm between reconstructed planes was selected for our clinical study.

The last step of the reconstruction process is the application of a deblurring algorithm to the tomosynthesis images produced by the shift-and-add technique. Traditional shift-and-add tomosynthesis requires little computational effort, but also results in substantial blur artifacts from structures outside of each plane of interest. In our tomosynthesis method, we use a deblurring algorithm called Matrix Inversion Tomosynthesis (MITS) that was developed in our laboratory (46, 48, 50, 52, 53, 79). The MITS technique uses linear algebra to solve identically for the blur from each reconstructed plane. In commercial tomosynthesis devices, filtered backprojection (FBP) (77) is more commonly used. Other investigators have also developed iterative deblurring methods (76) that provide high-quality reconstructions, but which take more computation time than MITS or FBP.

Chest Tomosynthesis for Lung Nodule Detection

There is growing interest in tomosynthesis for a number of clinical uses, including mammographic, orthopedic, and chest imaging applications, as evidenced by the increased number of tomosynthesis presentations at scientific meetings. As noted above, most of the interest in regard to chest tomosynthesis has been directed toward lung nodule detection.

There have been few published results from clinical trials of chest tomosynthesis to date. Two main studies have been published so far, one from our lab (5) and one from the group at the Sahlgrenska Academy of the University of Gothenburg, Sweden (32). We briefly summarize the results from these two studies below.

The Duke Experience

An NIH-funded clinical trial (R01 CA080490, “Tomosynthesis for improved pulmonary nodule detection”) was conducted at our institution for several years. This trial involved acquisition of digital PA and lateral chest radiographs, dual-energy tissue and bone images, and tomosynthesis data sets from 97 human subjects under an IRB-approved protocol. The chest radiographs and dual-energy images were acquired on a commercial flat-panel detector system (Revolution x/Qi, GE Healthcare, Milwaukee, WI, USA), and the tomosynthesis images were acquired on our prototype tomosynthesis system, described above. Patients scheduled for routine chest CT were contacted and consented for participation. Subjects with five or fewer noncalcified nodules were sought, although some subjects with more nodules and some subjects without nodules were also enrolled. Total radiation exposure for the chest tomosynthesis procedure was comparable to that of a conventional screen-film lateral radiograph (or two digital lateral radiographs).

We recently reported preliminary data from the first twenty-one subjects acquired (5). An expert consensus panel reviewed CT scans to confirm nodule presence, location and size. Three chest radiologists then independently reviewed tomosynthesis images and PA chest radiographs to confirm visualization of nodules identified by CT. Nodules were scored as: definitely visible, uncertain, or not visible. 175 nodules (diameter range 3.5 - 25.5 mm) were seen by CT and grouped according to size: < 5, 5-10, and > 10 mm. When we counted as true positives only those nodules that were scored as definitely visible, sensitivities for all nodules by tomosynthesis and PA radiography were 70% ($\pm 5\%$) and 22% ($\pm 4\%$), respectively, ($p < 0.0001$). Digital tomosynthesis showed significantly improved detection sensitivity for lung nodules in all three size groups, when compared to PA chest radiography. While this preliminary data is encouraging, and gives an upper bound for nodule detection sensitivity, these results must be confirmed by ROC analysis in the larger cohort of subjects, along with measures of specificity (currently ongoing). Examples from our data are shown in Figures 3 and 4.

The Sahlgrenska Academy Experience

A group of investigators from the Sahlgrenska Academy of the University of Gothenburg, Sweden recently reported results from a prospective human observer study of chest tomosynthesis. This trial was designed to compare tomosynthesis to conventional chest radiography for detection of pulmonary nodules, using multidetector CT as the reference standard (32). Subjects were recruited from a population undergoing CT to evaluate known or suspected chest disease. Forty-two subjects with and 47 subjects without lung nodules were included and received a chest tomosynthesis exam using a commercially available unit (VolumeRad, GE Healthcare, Milwaukee, WI, USA) and a conventional PA and lateral digital chest radiograph. Four thoracic radiologists with varying levels of experience with chest tomosynthesis evaluated the images and data were analyzed using a jackknife free-response operating characteristic curve (JAFROC) methodology. This study found that performance for lung nodule detection was significantly better for tomosynthesis than for conventional chest radiography. On average, three times as many nodules were detected by tomosynthesis than by chest radiography. Increase in detection sensitivity was greatest for nodules less than 9 mm in diameter. Interestingly, tomosynthesis resulted in a 50% increase in non-lesion detections (essentially false positives). This finding was attributed, to some degree, to a training effect; that is, less experienced observers tended to overcall nodules

more often than more experienced observers. In this study, the effective dose imparted for the tomosynthesis study averaged 0.12 mSv, about three times that of a standard digital PA and lateral radiograph chest exam.

Potential implementation strategies

Initial data from our institution and from the Sahlgrenska Academy thus suggest that tomosynthesis can substantially enhance sensitivity for lung nodule detection, when compared to chest radiography. This data, while promising, should be confirmed in larger, preferably multicenter clinical trials. In particular, the finding that tomosynthesis could lead to an increased number of non-lesion detections (32) needs to be evaluated further, as this effect could blunt any potential advantages of the technique. Clearly, more research is needed to establish a clinical role for tomosynthesis in the detection or evaluation of lung nodules.

Despite its potential, tomosynthesis is a new technique, and therefore, there is no historical perspective to guide its integration into the clinical practice of chest radiology. Questions arise as to how it should be used, and on which patients, and how it might potentially be used in conjunction with both chest radiography and CT. We can envision at least four different potential strategies or scenarios for incorporating tomosynthesis into the clinical arena. All strategies have potential benefits and drawbacks.

1. Additional or replacement test in **ALL** patients undergoing chest radiography—

In this scenario, chest tomosynthesis would either be performed in addition to, or in lieu of, conventional chest radiography (PA and lateral) in ALL patients referred for this examination. The potential benefit is the improved detection of pulmonary nodules (and potentially other pathologies) with chest tomosynthesis than with conventional chest radiography. This of course, presumes that further research substantiates not only that tomosynthesis improves lung nodule detection, but that its use also results in improved patient outcome, compared to chest radiography. This approach does involve, however, additional radiation to the patient and additional cost to the healthcare system. Radiation exposure could be reduced, however, if it could be shown that tomosynthesis obviates the need for the lateral radiograph. In that case, tomosynthesis exposure would be comparable to a conventional PA and lateral exam. The workflow issues surrounding substitution of an often-performed exam consisting of two images with an examination comprised of up to 70 images would need to be carefully addressed. And, again, issues surrounding false positive detections must be resolved.

2. Additional or replacement test in **SOME** patients undergoing chest radiography—

In this scenario, some (presumably high-risk) patients would receive a tomosynthesis examination, either in addition to or in lieu of a conventional chest radiographic examination (PA and lateral). This approach again presumes that research substantiates not only improved detection of lesions in these groups, but improved outcome with tomosynthesis as well. One potential target population is current or former smokers at risk for lung cancer. There has been considerable interest in recent years in using low-dose CT to screen high-risk patients for lung cancer (23-31). The merits of CT lung cancer screening are, of course, debated and, as yet, no consensus has emerged. However, if lung cancer screening with low-dose CT is shown to be beneficial in the ongoing NIH-sponsored National Lung Screening Trial (23), it is possible that tomosynthesis might also have merit for lung cancer screening. Tomosynthesis could even prove more useful than CT by detecting a high percentage of so-called “actionable” nodules at lower cost than CT. Other potential “target populations” might include individuals at high risk for metastatic disease. A targeted approach to implementation of chest tomosynthesis would seem to have greater

merit than a more general implementation strategy (scenario #1) by maximizing chances for improved patient outcomes and by minimizing (to whatever degree possible) cost, radiation dose and workflow issues.

3. Evaluation of suspicious lesions seen by conventional chest radiography—

CT is the current standard for characterization of opacities identified on chest radiographs (80-82). Yet, many “nodules” detected on chest radiographs prove not to be nodules at all (rib fractures, confluent vessels, etc). Worse, incidental findings are often discovered in these patients at CT, necessitating further costly evaluation. In this implementation scenario, tomosynthesis would be used as a problem-solving tool to obviate unnecessary CT. Suspicious opacities noted on chest radiographs that cannot be definitely identified as pulmonary nodules would undergo tomosynthesis. Only those lesions that proved to be true nodules would proceed to CT for further characterization. This scenario is similar to the older strategy employed in some institutions of sending patients with suspicious opacities to fluoroscopy to exclude nodule mimics and benign disease. This approach has the potential to reduce cost and radiation exposure by substantially reducing referrals to CT.

4. Follow-up of known nodules—Many nodules identified by either chest radiography or CT require follow-up in order to determine whether or not they are malignant (83, 84). Currently, most nodule follow-ups are performed with CT. In this implementation scenario, tomosynthesis would be used in place of CT to follow pulmonary nodules previously identified by chest radiography or CT. This approach would involve a savings in radiation dose and expense over following the nodules with periodic CT scans, but might fail to detect new nodules that are smaller than the sensitivity threshold for tomosynthesis (estimated to be about 4-mm in diameter). The accuracy of tomosynthesis for detecting changes in lung nodule size or density would first need to be determined.

Future Directions

The main application of chest tomosynthesis to date has been in improving detection of pulmonary nodules, but it may also have other potential uses in thoracic imaging. Such potential uses include, but are not limited to, evaluation of suspected interstitial lung disease, early detection of infection in immunocompromised patients, detection of subtle pneumothoraces, detection of cardiac or coronary artery calcification and evaluation of ribs and spine for fractures, metastases or other osseous lesions. These uses will require further clinical study. Further, iodinated-contrast enhanced applications within the chest have yet to be explored.

Commercial tomosynthesis systems for chest imaging are currently available. These commercial products use a conventional x-ray tube, a flat-panel detector mounted on a wall stand or table top, and a modified and motorized overhead tube crane. Tomosynthesis images are acquired immediately following a conventional PA chest radiograph without repositioning the patient. A number of installed sites are acquiring chest tomosynthesis images using these devices, and within the next year or two we anticipate that further clinical experience with the devices will guide the development of optimum clinical utilization strategies.

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Figure 1. Basic components of a chest tomosynthesis device

A computer-controlled motorized tube crane moves the x-ray tube to a series of positions along a vertical path, acquiring a projection image on a flat-panel detector at each position. Control circuitry coordinates the tube mover, digital detector, and x-ray generator. A workstation produces the tomosynthesis reconstructed images.

Figure 2. Shift-and-add technique for tomosynthesis image reconstruction (reprinted from (6), by permission)

A. In this example, an x-ray tube moves to five discrete positions. Objects in Plane A and Plane B are projected at different locations in each image due to parallax.

B. The five projection images are shifted and added together to yield a composite image with either the objects in Plane A or Plane B in sharp focus, depending on the magnitude of the shift.

Figure 3. Pulmonary metastases

- A. Posteroanterior chest radiograph shows bilateral pulmonary nodules.
- B. Chest tomosynthesis image reconstructed through the mid-chest shows at least two nodules (arrows) not seen on PA radiograph (A). Note excellent depiction of vasculature, airway and ribs.
- C. Chest tomosynthesis image reconstructed through the posterior chest shows additional nodule (arrow) superimposed over left hilum on PA radiograph (A).
- D. CT (lung window) images confirm three nodules (arrowheads) seen on tomosynthesis images (B, C), but not clearly depicted on PA radiograph (A).

Figure 4. Pulmonary metastases

A. Posteroanterior chest radiograph shows findings of prior partial right lung resection for metastectomy and one left upper lobe nodule (arrow).

B. Chest tomosynthesis image reconstructed through the mid-chest shows at least one nodule (black arrow) not seen on PA radiograph (A). Note left upper lobe nodule (white arrow).

C. Chest tomosynthesis image reconstructed through the posterior chest shows an additional left lower lobe nodule (arrow) not seen on PA radiograph (A).

D. CT (lung window) images confirm two nodules (arrowheads, bottom two panels) seen on tomosynthesis images (B, C), but not clearly depicted on PA radiograph (A). Note left upper lobe nodule (arrowhead, top panel) seen on both PA (A) and tomosynthesis images (B).