Chest Radiography: New Technological Developments and Their Applications

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Abstract

Digital chest radiography is still the most common radiological examination. With the upcoming three-dimensional (3D) acquisition techniques the value of radiography seems to diminish. But because radiography is inexpensive, readily available, and requires very little dose, it is still being used for the first-line detection of many cardiothoracic diseases. In the last decades major technical developments of this 2D technique are being achieved. First, hardware developments of digital radiography have improved the contrast to noise, dose efficacy, throughput, and workflow. Dual energy acquisition techniques reduce anatomical noise by splitting a chest radiograph into a soft tissue image and a bone image. Second, advanced processing methods are developed to enable and improve detection of many kinds of disease. Digital bone subtraction by a software algorithm mimics the soft tissue image normally acquired with dedicated hardware. Temporal subtraction aims to rule out anatomical structures clotting the image, by subtracting a current radiograph with a previous radiograph. Finally, computer-aided detection systems help radiologists for the detection of various kinds of disease such as pulmonary nodules or tuberculosis.

Keywords
- digital radiography
- detectors
- image processing
- advanced processing
- dual energy subtraction
- digital bone suppression
- temporal subtraction
- computer-aided detection

The conversion from conventional screen film to digital technique took place in the 1980s and became clinically feasible after the introduction of storage phosphor detector technique. Organizational advantages as instant availability of the images in multiple locations eased the acceptance by clinicians. From the radiologists' viewpoint options for image processing and lower vulnerability to over/underexposure represented major progress. Moreover, digitization of radiographic examinations represented the last step toward a complete digital imaging department since other cross-sectional imaging techniques such as the computed tomography (CT) or magnetic resonance tomography had been from beginning in a digital format.

Today, the process of optimization of processing seems more or less finalized. Differences between techniques and manufacturers have become very small and there appears to be a common sense for what is considered an "optimal radiographic image." Recently, within the area of processing, the focus has dramatically changed. Elaborate processing schemes including dual energy subtraction or digital bone suppression, temporal subtraction or tomosynthesis (see Chapter 2 "Chest Tomosynthesis: Technical Principles and Clinical Update" in this issue) are increasingly available. They all have the goals to decrease distracting anatomic noise in the image, to improve perception of pathology and decrease inter- and intrareader variability. Computer-aided detection (CAD) schemes analyze morphological image features in the background to provide the radiologists with candidate lesions in areas that need increased attention.

This article will provide an overview over the present available detector systems with special emphasis on their capabilities with respect to dose efficiency. Principles of processing will be summarized including most modern elaborate processing options that go beyond the optimization of image quality but are designed for detection support and diagnostic aid.

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Detector Technology

A variety of detector technologies has been exploited in modern digital radiography; each coming with different characteristics in terms of physical performance and thus image quality, different levels of dose efficiency and processing options, and last but not the least various organizational and financial aspects.

Basically three types of detector systems can be differentiated that are in use for radiographic applications today (1) storage phosphor radiography (computed radiography, CR), (2) flat panel direct radiography (DR), and (3) slot scanning charge coupled devices (CCD) technology, the latter being the least applied one.

Computed Radiography (Storage Phosphor Radiography)

CR technology was the first detector technique for digital radiography to be introduced in the early 1980s. It was immediately accepted by the radiological and clinical community due to its organizational advantages and the fact that this cassette-based system could be used with already existing hardware components.

The name “storage phosphor” refers to the fact that the image information (relief of absorbed radiation) is stored within the detector layer of photostimulable phosphor material (BaFX: Eu2 +). Absorption of radiation leads to excitation of electrons that are trapped within the crystalline structure, and only illumination of the image plate to a thinly focused laser light during a dedicated read-out process causes the trapped electrons to relax to their ground state while emitting light. The stimulated light emission is collected via an optically efficient light guide, converted to electronic current by a photomultiplier, logarithmically amplified, filtered, and finally digitized using a 12-bit analogue-to-digital converter.

In its first version after the introduction CR offered limited options for reducing the radiation dose per exposure as compared with the film screen. In fact image quality was characterized by relatively high noise especially in high absorption areas. Detector material and read-out technology, however, were continuously improved over the following years.[1,2] Most recent and more radical innovations, such as the dual read-out technology or needle crystalline detector technology have further attributed to substantial improvement of dose efficiency that is now approaching that of flat panel technology and by far exceeding that of conventional film/screen combination with a sensitivity (speed) of 400.[3–5]

Storage phosphor needle-like detectors use a more efficient X-ray absorption material (CsBr:Eu2 +) and are structured in needle-like columns instead of small crystals. The result is a marked reduction of lateral scattering of the emitted fluorescent light allowing for increasing detector thickness and thus improving dose efficiency without losing geometric resolution.[3]

“Dual-sided read-out” captures the laser-stimulated phosphorescence light from both sides. This dual-sided approach can access a larger proportion of the trapped electrons and as a result achieve a more complete read-out of the latent image. The result is an improved signal and signal-to-noise characteristics for a given absorption of radiation within the detector. The dual-sided read-out does not affect the spatial resolution since the amount of scattering of light remains unaffected. Literature reports an increase of fractional X-ray absorption efficiency of the image plate by 50% through the dual-sided read-out. Physical and clinical evaluations confirmed a substantial increase in image quality.[4,5]

CR used to be a cassette-based system and is as such still in use, for example, in intensive care wards. It is also available in dedicated chest stands or Bucky units that offer automatic read-out and require no manual interaction with the cassettes. Also the needle-type detector is available as cassette-based system as well as system integrated in Bucky and fluoroscopy units.

When using CR systems or reading comparison studies that include CR technique it is very important to pay attention to the type of detector (needle vs. powder storage phosphor), which generation of powder storage phosphor plate, and which read-out system has been used. The pure description of CR is too nonspecific and refers to various systems with a broad range of performance.[6]

Direct Radiography (Flat Panel Detector Systems)

Flat panel detector systems—also referred to as DR—are characterized by a direct read-out matrix of electronic elements that are made of thin layers of amorphous silicon thin-film transistors (Si–TFT elements) that are deposited on a piece of glass. The TFT layer is coupled with an X-ray absorption medium responsible for capturing the radiographic image information.[7,8]

Depending on the material used, there are two types of DR detectors.

1. Detectors using a scintillator (cesium iodide, CsI or gadolinim oxysulphide, GOS) and light-sensitive photodiodes are called indirect conversion TFT detectors or *optodirect systems*. Similar to the CR technology, the absorbed radiation is transferred into light signals in the CsI layer. CsI–TFT systems are widely applied for chest and skeletal radiography and are also amenable to real time display. More recently, mobile DR units have also become available, which are suitable to be used at the bedside.
2. In direct conversion systems, the detector elements consist of condensator elements made up of amorphous selenium (or other semiconducting materials) that is deposited on the TFT array. Absorbed X-ray energy is directly converted into charge, obviating the intermediate step of a scintillator to provide conversion to visible light. These systems are not amenable to real-time imaging due to the tendency to produce persistent latent images. They are mostly applied in mammography units because they provide high dose efficiency for the high frequency ranges needed in mammography.

DR has markedly higher dose efficiency as compared with first generations standard CR (►**Fig. 1**). As compared with the most modern CR units, however, differences with respect to image quality and workflow organization become much less

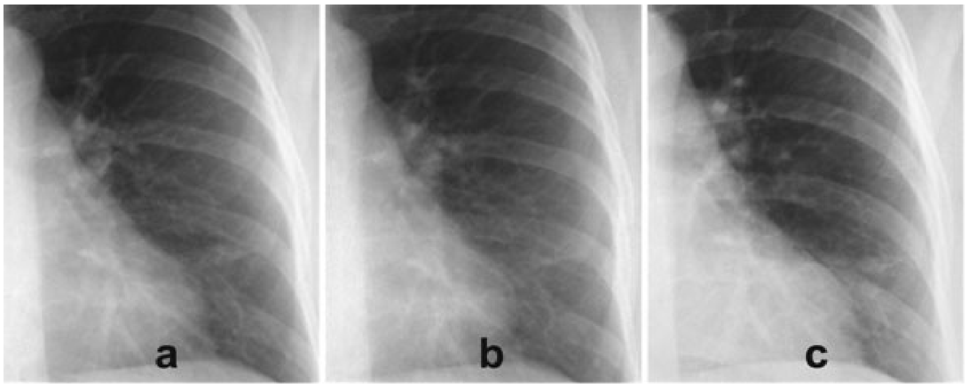

Fig. 1 Images of the left lower lung demonstrates the potential of dose reduction of direct radiography (DR) as compared with computed radiography (CR, powder). Image b (DR) was obtained with 50% of the dose compared with a (DR) and c (CR).

prominent. It is therefore important to consider, which type of storage phosphor system (detector generation, read-out) is used. DR (CsI/TFT) systems are amenable to high frame rates (up to 30/s) making them suited for fluoroscopy applications also. By integrating acquisition, read-out and processing into one system, throughput and workflow can be optimized. Integrated systems are available for both CR and DR. When CR is used as a cassette-based system, for example, at the bedside, these advantages (e.g., immediate availability of pre-read, no cassette handling) perish.

CCD and CMOS-Based Detectors

CCD and complementary metal oxide semiconductor (CMOS) devices were initially suffering from lower dose efficiency that could not compete with DR or CR systems. They also use scintillating phosphor as an absorption medium; emitted light is directed to multiple CCD or CMOS cameras that form the radiograph. Various optical arrangements including lenses or fiber-optic tapers are used for the coupling between the phosphor layer and the mostly relatively small cameras.

As only a fraction of the light could be captured by the cameras, image formation was less efficient with respect to signal-to-noise characteristics. This limitation was even more obvious for clinical applications that require a large area (e.g., chest). Recent developments markedly improved the coupling efficiency by using larger sensors and improved phosphor efficiency, making these systems also suitable for high quality chest- and large area skeletal radiography. CCD and CMOS systems have a wider distribution in the United States, but are only scarcely applied in Europe.

Irradiating the body by a sliding slit beam instead of irradiating the whole body at once is called the slot-scan technology and provides excellent scatter rejection. The increased signal-to-noise characteristics yielded by scatter reduction effectively compensates for the 2.5 times lower intrinsic detective quantum efficiency (DQE) of CCD technology allowing for a successful combination of slot-scan and CCD technology. Advantages of this CCD slot-scan technology are especially prominent for the mediastinum: both CsI–DR at 75% dose reduction and CCD slot scanning at 50% reduction outperformed a standard CR system.[9] Though these systems provide excellent image quality at reasonable doses, they did not find a broad international application, most likely to specific hardware requirements and the fact that they are exclusively amenable to chest imaging.

Physical Parameters of Detector Systems that Determine Image Quality

Dynamic range is defined as the of absorption differences that can be accommodated by the detector system and thus contribute information to the recorded image.[1] In thoracic imaging the absorption difference between normally ventilated lung and mediastinal soft tissue is 1:80. In screen-film radiography the dynamic range was defined by the radiographic response of the film and was rather limited (1:10) as illustrated by the somewhat too white mediastinum or too black lung. In digital radiography (true for CR and DR), the maximum signal capability is set by the detector medium itself and its read-out mechanism, the minimum signal capability is set by the image noise and the greyscale discrimination capability of the system. The dynamic range of digital radiography (CR and DR) is about 400 times wider as conventional film meaning that digital systems can obtain image information over a much wider range of entrance doses.

The spatial resolution of an image detector refers to its ability resolve two (or more) small high-contrast image features as independent entities.[1] The spatial resolution is influenced by many factors such as the detector medium itself (e.g., needle channeled CR vs. powder crystals CR), the detector thickness, the size of the laser beam, the pre- and postprocessing and finally the pixel size. CR plates offer a pixel sampling interval between 0.5 and 200 µm, DR systems between 140 and 200 µm. More important for visual discernibility of, for example, parenchymal details, however, is the relationship between detail size and detail contrast, described in the modulation transfer function (MTF): the higher the MTF the smaller the details an imaging system displays with visually discernible contrast. Especially processing has a vast influence on the MTF, and is optimized to improve the rendition of fine and small detail structures on

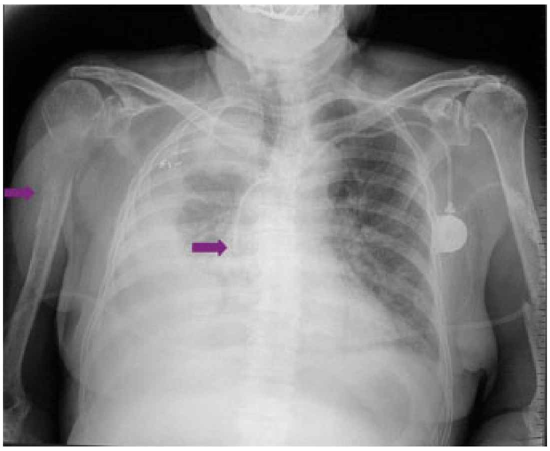

Fig. 2 The wide dynamic range of digital imaging technique allows for optimized display of structures in high- and low-absorption areas, for example, the tip of the central venous catheter (centrally located arrow), signs of vascular congestion in the left lung, and the right-sided pathologic subcapital humerus fracture (peripherally located arrow).

one side and increase visualization of ill-defined low contrast lesions on the other side. Therefore, it is inadequate to focus on the pixels sampling interval alone. Multiple studies could show that there is no diagnostically relevant difference between 2K and 4K CR systems (pixel sampling difference 100 and 200 µm), for chest abnormalities, given an appropriate processing.

DQE is regarded as the best single indicator to describe the performance of digital radiographic systems.[10] The DQE of an imaging system refers to the ratio between the SNR at the entrance to the image detector (flux of X-ray photons incident upon the image detector) and the SNR recorded by the image detector (the value which is computed from the output data). Ideally that value would be 100% (what goes in also comes out) but depending on the amount of extraneous noise sources in the image detector itself the DQE will be less than 100%. The greater the value of DQE, the more efficiently the detector records X-ray image information. The magnitude of DQE is influenced by the effective beam energy, the detector entrance dose level, the detector system itself and the targeted image frequencies.

Image Processing

One of the most important advantages of all digital radiographic detectors is their wide dynamic range making them less vulnerable toward under- or over exposure. Together with adequate image processing, these systems produce over a wide range of exposures adequate image quality (►**Fig. 2**). A process called signal normalization—automatically running in the background—yields images with adequate density and contrast independent of acquisition dose (►**Fig. 3**). However, this harbors advantages and disadvantages: visual control of acquisition dose is more or less lost and there is a certain risk for over exposure (e.g., in pediatric units)[11] which will even be awarded by excellent image quality. A too strong dose reduction on the other hand leads to a loss of fine detail because of increased image noise (►**Fig. 4**). Thus—though less critical as compared with traditional film/screen radiography—there are limitations for how much the dose should be increased or decreased.

Image processing critically influences image quality and thus diagnostic performance: while adjustments of gradation curves influence overall image contrast and density, frequency processing enhances local contrast or even selectively enhances structures of a certain size or contrast.[12] Unsharp mask filtering is the simplest type of frequency processing but

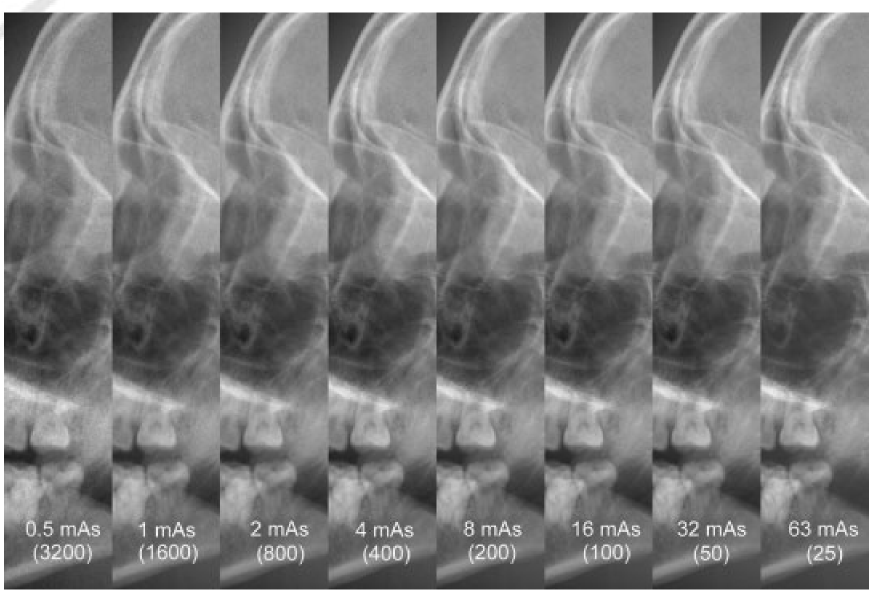

Fig. 3 Images of a scull phantom. Over a dose range between 0.5 and 63 mAs (factor > 100) digital technique is able to yield images with comparable and diagnostically useful contrast and density. Though images on the left side (low dose) have a higher noise and therefore demonstrate a less sharp delineation of the linear details compared with images on the right side.

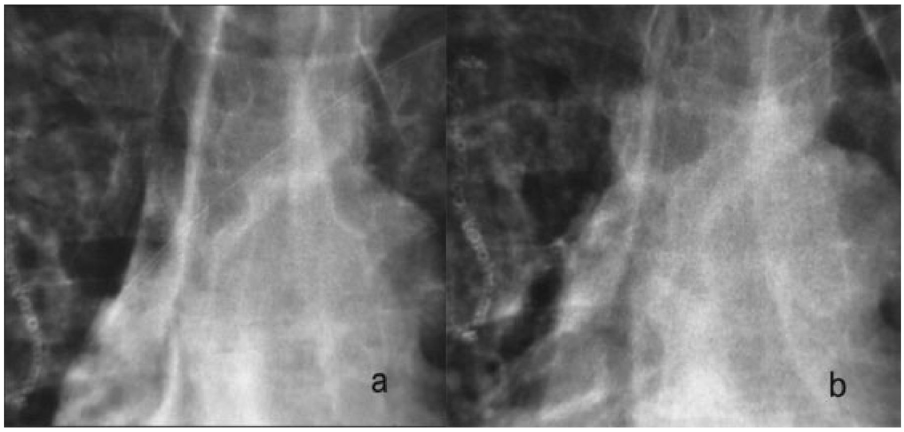

Fig. 4 Image (b) was obtained with one-third of the dose used for image (a). Image contrast and density appear to be comparable. However, the ratio between signal and noise became too low in image b to capture the linear density of the intravenous catheter. Thus, a too strong dose reduction will lead to loss of detail and thus potentially diagnostic information.

has the disadvantage that stronger filter settings lead to (edge) artifacts.

Most vendors have made the transition to multifrequency processing algorithms (e.g., MUSICA, UNIQUE, MFP).[13,14] Multifrequency processing makes it possible to separately enhance and suppress image structures dependent on their contrast (amplitude), their size (spatial frequency bands), and their background density (mediastinum vs. lung).

The desired result is an "image harmonization" with a more transparent mediastinum and improved visualization of low contrast structures throughout the chest with simultaneous display of soft tissue and osseous structures and preserved high resolution for low contrast differences in the lung (►**Fig. 5**). Today, there is a general agreement that a too strong enhancement of edges along anatomic structures (e.g., vascular shadows) produce diagnostic misinterpretation (e.g., of cardiogenic congestion or interstitial lung disease [ILD]), and may in fact lead to loss of diagnostic detail (►**Fig. 6**).

Advanced Processing

Advanced processing refers to the techniques that are aimed to aid detection performance. They produce processed images that differ from the original images in such a way that they are used as an adjunct to the original images with the idea to enhance image formation or draw the observer's attention to a certain area or structure. All of these techniques are designed to reduce overlapping potentially distracting structures (e.g., bones) or highlight areas of suspicion (e.g., circles around nodules produced by CAD) with the ultimate goal to support the detection performance of the observer.

Techniques such as digital bone suppression, dual energy acquisition or tomosynthesis are designed to reduce overlying structures, for example, bones, that way reducing the "anatomic noise" and providing the reader with an unobscured display of the lung parenchyma. Tomosynthesis goes a step further, displaying a subvolume of the lung similarly to CT that way reducing projection effects. This technique will be

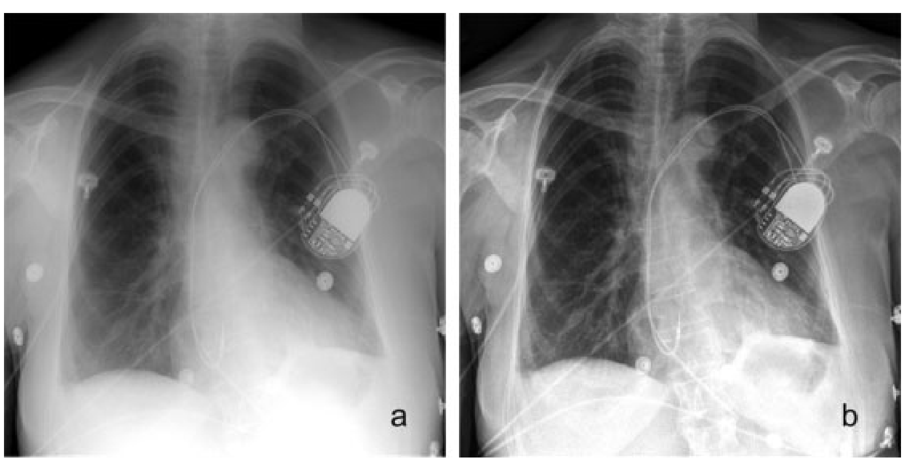

Fig. 5 Desired effects of processing are compression of the dynamic range with increased transparency of the mediastinum and simultaneously increased detail contrast in the lung parenchyma (visible in [b] as compared with [a]).

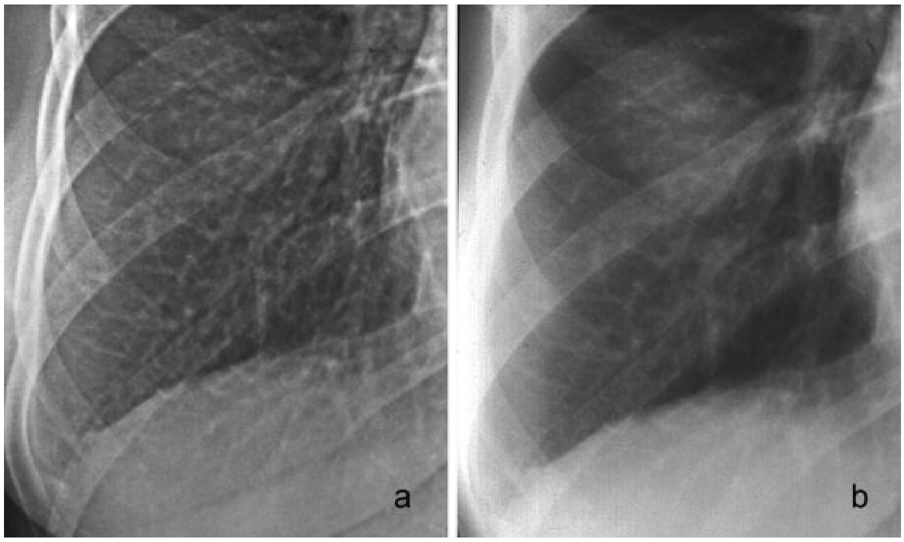

Fig. 6 Unwanted effects of image processing. Suboptimal processing parameters (a) lead to too strong enhancement of vascular structures and noise but obscuration of the faint density caused by an interlobular effusion (seen in b).

discussed in Chapter 2 "Chest Tomosynthesis: Technical Principles and Clinical Update". Temporal subtraction and CAD highlight areas of suspicion that subsequently need to be accepted or dismissed by the radiologist as real pathology.

Bone Subtraction

Chest radiographs are complex radiological examinations to review. Multiple anatomical structures contribute to a complex two-dimensional (2D) image of a 3D volume. This high level of so called "anatomical noise" is one important factor contributing to the difficulty of interpretation of chest radiographs. Bones have shown to be a major contributor to this noise, and are an important cause of missed lung nodules.[15,16] Therefore, several techniques have been proposed to suppress overlying bone structures; this can be achieved either digitally or using a dedicated dual energy acquisition technique.

Dual Energy Radiography

Dual energy radiography is based on the principle that radiation absorption by tissues is dependent on the energy of roentgen photons. At high energy level (> 100 kVp) absorption of photons differs not much for bone and soft tissue. At lower energy levels, however, photoelectric absorption is much more effective for tissue containing calcium and thus bones. This effect is used to produce images mainly displaying soft tissue information and images mainly displaying calcified structures as ribs, spine, or calcified nodules.

Two techniques of energy subtraction (ES) can be distinguished: single shot ES radiography and dual shot ES radiography.

Dual-shot ES radiography uses two exposures: one at a high and one at a low energy level. Subtraction of these two radiographs using specific weighting factors generates a "soft tissue image" and a "bone image." The images have usually high quality with high contrast and low image noise. But the short interval of 150 to 200 ms between the two acquisitions can cause motion artifacts, mainly caused by movement of the heart, diaphragm, and hilar vessels. Also the need for two acquisitions slightly increases the total dose of the examination.

Single-shot ES radiography requires only one exposure. In one cassette are the two detector plates separated by a copper filter. While the first detector plate is radiated by the full radiation spectrum producing a "normal" radiograph, the second detector plate is only radiated by a high energy radiation spectrum since the low energy photons were absorbed by the copper filter. The image detected by the second plate has low bone contrast, and is noisier than the radiograph detected by the first plate. Subtraction of the two acquired images using specific weighting factors produces again a soft tissue and a bone image. Since the image detected by the second plate is noisier, also the resulting images suffer from higher image noise and thus lower overall image quality. In opposite to the dual shot technique they do not suffer from subtraction artifacts.

Several studies testing these dual energy techniques have been performed. ROC analysis in multiple observer studies showed an increased performance for the detection of lung nodules with help of dual energy images (soft tissue image and bone image; ►**Table 1**).[17–23] Studies found an increase of sensitivity that varied between 5 and 19%. Also few studies failed to prove added value of dual energy images, mainly because a decrease in specificity.[24,25] Besides solid lung nodules also part solid nodules and ground glass opacities could be more easily detected with dual energy radiographs.[18,20,23] When calcification of nodules can be identified on the bone images, further CT examinations might not be needed.[26] However, small amounts of calcium may not be seen with dual energy radiography. The bone image can also be used to clarify other calcified disease like pleural plaques and mediastinal calcified nodules.[27] Also some studies found

Table 1 Overview of studies using digital bone suppression or dual energy subtraction images for the detection of lung nodules

Author	Journal	System	Technique	Cases	Observers	Average nodule size	Significance
BSI (software)							
Li et al (2012)[a]	Eur Radiol	Riverain Technologies	Software	56	8	28 (12–60)	b
Freedman et al (2011)	Radiology	Riverain Technologies	Software	368	15	18.8 (4.7–36.7)	b
Li et al (2011)	Radiology	Riverain Technologies	Software	80	10	20 (9–30)	b
Li et al (2011)	AJR Am J Roentgenol	Riverain Technologies	Software	151	3	16 (6–30)	c
Dual energy							
Li et al (2011)	Radiology	Fuji Medical Systems	Single-shot	80	10	20 (9–30)	b
Oda et al (2010)	Clin Radiol	GE Healthcare	Dual-shot	41	8	15 (7.1–20)	c
Szucs-Farkas et al (2008)	Eur Radiol	Fuji Medical Systems	Single-shot	102	5	10 (5–116)	ns
Rühl et al (2008)	Eur Radiol	GE Healthcare	Dual-shot	100	5	11 (3–45)	ns
Li et al (2008)	AJR Am J Roentgenol	Fuji Medical Systems	Single-shot	35	6	15.6 (7–22)	b

Abbreviations: AJR Am J Roentgenol; AJR. American journal of roentgenology; BSI, bone suppression imaging; Clin Radiol, Clinical radiology; Eur Radiol, European radiology; ns, nonsignificant.
Note: Riverain Technologies (Miamisburg, OH); Fuji Medical Systems (Stamford, CT); GE Healthcare (Waukesha, WI).
[a]Study used subjects with focal pneumonia instead of lung nodules.
[b]$p < 0.01$.
[c]$p < 0.05$.

beneficial effects for the detection of cardiac calcification.[28,29] Besides, radiopaque foreign objects, like medical devices, catheters, drains, silicone breast implants, are more easily seen (►**Fig. 7**). No improvement was found for the detection of rib fractures based on the bone image.[30]

There is no clear preference for single or dual shot energy subtraction techniques for the detection of lung nodules. One study explicitly compared dual- and single shot techniques and could not demonstrate a significant difference in the detection of lung nodules between the two techniques.[26]

Despite the mainly positive results, both techniques (dual shot and single shot) have never found their way into broad clinical application. Both techniques require specific hardware and software facilities, meaning that this technique cannot be applied using already existing radiographic equipment. For a long time, the image quality of the soft tissue and bone images was considered insufficient. The quality of these images, however, could be substantially improved over the time making them a useful adjunct, especially for the detection of focal disease. It is most likely a combination of all—the

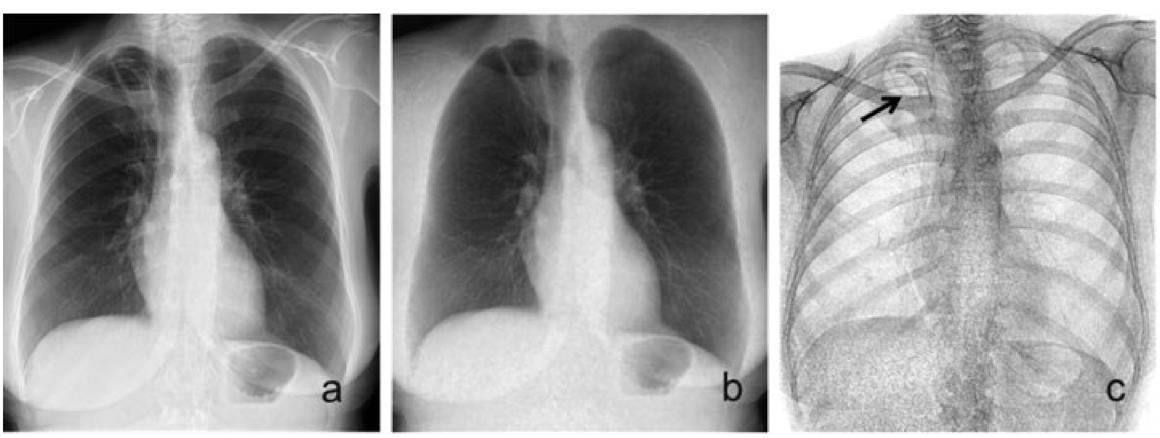

Fig. 7 PA radiograph (a) with circular opacification in the right upper lobe suspicious for a cavitation. Soft tissue (b) and bone image (c) produced by dual energy subtraction technique demonstrate a linear scarring (b) and a radio-opaque vascular stent (c, arrow) as explanation for the circular opacity. Image courtesy of Peter Vock, Chief of Diagnostic, Interventional, and Pediatric Radiology, University Hospital of Bern, Bern, Switzerland. PA, posterioranterior.

need for specific hardware, the increasing availability of CT and the need to integrate an additional soft tissue image into the reading process—that has contributed to the still somewhat limited use of this technique.

Bone Suppression

The need for special hardware is an important drawback for dual energy radiography. Therefore, investigators focused on digital removal of bony structures in the chest radiograph using dedicated software applicable to already existing radiographic equipment (►**Fig. 8**). Advantages of such a solution are that image quality is not suffering from subtraction artifacts (by motion in dual shot energy subtraction), no increase in dose for the patient and no special hardware is required. The software product can be integrated in the picture archiving and communication system. Disadvantage is that the software algorithm is designed to detect solely bone structures and not all structures with high density. Therefore other high calcium structures, such as calcified nodules or old rib fractures, are not recognized and not suppressed, as in energy subtracted images.

First articles about a bone suppression technique by a computer algorithm have been published in 2006.[31,32] Studies using the bone suppression technique found an increase in performance for the detection of lung nodules (►**Table 1**).[17,33,34] The largest observer study which incorporated 15 observers and 368 cases found an average increase in sensitivity of 17%, but also a loss in specificity of 4%.[33] The software solution might also be used for the detection of other abnormalities. Li et al[35] found a significant increase for the detection of focal pneumonias, and improved detection of other disease is conceivable. Artifacts of the suppression techniques can cause pseudolesions, which result in a somewhat lower specificity. Most artifacts are caused by overprojection of multiple structures, such as in the apical regions where both the clavicle and the first rib obscure the lung field (►**Fig. 9**).

One of the articles also compared bone suppression imaging software with dual energy bone suppressed images.[17] In an observer study 10 radiologists searched 80 chest X-rays (CXRs) for lung nodules first unaided, followed by and interpretation of the digitally bone suppressed image, and finally with dual energy image. Biggest increase in performance was seen with the help of the dual energy bone suppressed images, although both techniques showed significant improvement over original chest radiographs.

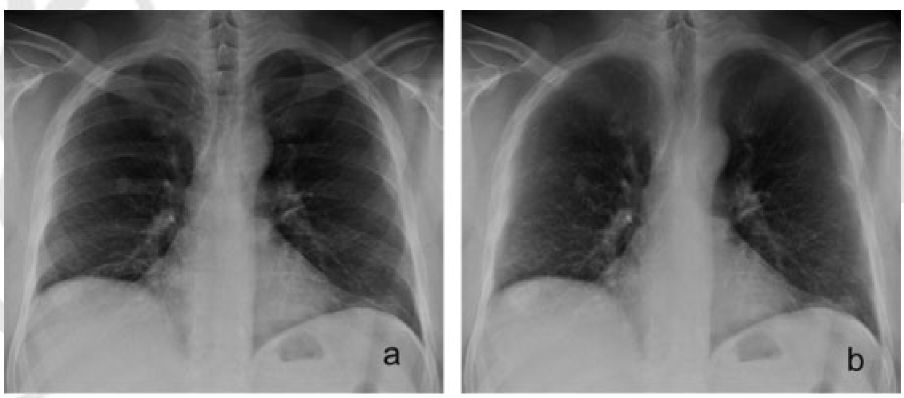

Fig. 8 PA radiograph with a solitary nodule in the right lung. The nodule is overlapped by a projection of the seventh posterior rib. Digital bone suppression (Riverain Technologies, Miamisburg, OH) produces a bone suppressed image, where the rib is perfectly suppressed without suppressing the lung nodule. PA, posterioranterior.

Fig. 9 Bone suppressed image generated from original radiograph (a), (b), generated from original radiograph (a), shows a pseudolesion in the right apex, due to incomplete suppression of calcification of the first rib.

Considering that digital bone suppression is still a relatively young technique, more beneficial effects might be demonstrated in the future. Artifacts could be minimized and with further experience with this technique artifacts may be more easily denied. Clinical studies will have to show this effect.

Computer-Aided Detection

The approach of CAD techniques is to decrease the intrinsic limitations of human perception, by alerting the observer to suspicious areas in a CXR.

First computer analysis techniques of chest radiographs were already published in the 1960s.[36,37] Several generations of CAD software have been introduced and most of them focusing on the detection of nodules, meaning focal densities smaller than 3 cm. Other indications, less well advanced computerized detection systems so far, refer to the detection of spine fractures, heart size, ILD, emphysema, and tuberculosis (TB).

Development of techniques for the automatic detection of lung nodules in chest radiographs started in the 1970s.[38,39] Matsumoto et al[40] were one of the first to apply a CAD scheme on a series of radiographs with lung cancer. CAD was able to reach a sensitivity of 62%, which was comparable to the radiologists. On the other hand, the system produced an average of 15 false positive (FP) findings per image leading to an overall loss of performance of radiologists because of acceptance of too many FPs.[41] In a study with a simulated improved performance of the same CAD with a sensitivity of 80% at 1 FP/image, radiologists did benefit from the CAD system.[41] These early studies already pointed out to the main challenge for radiologists when using CAD, namely, to take advantage of CAD by detecting more focal lesions that would have been otherwise missed without losing specificity by accepting too many FP candidate lesions.

Since then CAD has been applied on multiple sets of radiographs, showing the potential for detection of lesions that were missed by human observers.[42–44] Sensitivities ranged from 35% at 5.9 FP/image to 49% at 1.8 FP/image for these missed lesions.

Still the various CAD systems are difficult to compare, since training and testing of the system is often done with different data and studies use different sets of lesions. But multiple studies have reported their CAD performance on a publicly available database from the Japanese Society of Radiological Technology.[45] Looking at the CAD performances on this database, CAD evolved quickly from a sensitivity of 35% with 6 FP/image in 1999 to a sensitivity of 75% with 0.5 FP/image in 2012 (►**Fig. 10**).[46–53] Compared with an average sensitivity of 70% at a specificity of 81% for radiologists for this database, CAD is approaching the performance of an average radiologist.

As mentioned above, the effect of CAD on observer performance highly depends on its ratio between true and FP candidates. Although, significant improvements are made over the last 10 years, CAD is still not able to achieve performance of a human observer. Therefore, CAD is designed to be used as a second reader. This means that the human observer, after his first evaluation, can ask CAD to show suspicious regions. The human observer than has to accept or neglect the suggested findings of the computer. Several studies with different CAD systems have been performed to investigate the added value of CAD as a second reader. These studies reported variable results. While some studies were able to demonstrate an increased accuracy for the detection

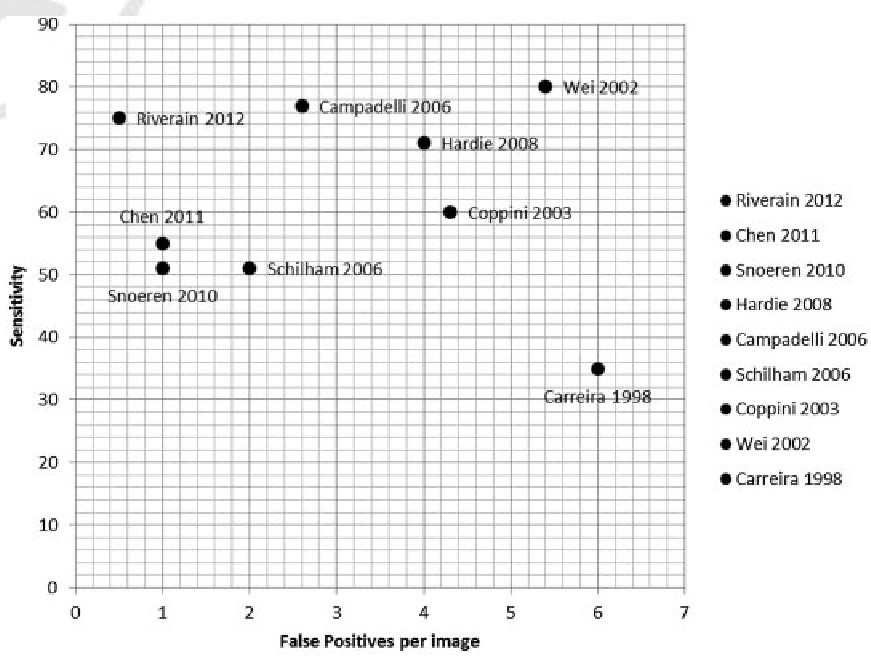

Fig. 10 Improvement of CAD. Published performances of CAD systems applied on a publicly available database from the Japanese Society of Radiological Technology (JSRT). Over the past 15 years performance of CAD systems dramatically increased from a sensitivity of 35% at 6 FP/image to a sensitivity of 75% at 0.5 FP/image. CAD, computer-aided detection; FP, false positive.

Table 2 Overview of the most recent studies evaluating computer-aided detection for lung nodules

Author	Journal	System	Cases	Observers	Average nodule size	CAD stand alone Sensitivity (%)	FP per image	Significance
Lee et al (2012)	KJR	EDDA	200	10	15.4 (7–20)	59	1.9	ns
Kligerman et al (2013)	J Thorac Imaging	Riverain Onguard 5.1	296	11	21 (8–41)	49	1.8	a
De Boo et al (2011)	Acad Radiol	EDDA	113	6	(5–15)	47	1.7	ns
Xu et al (2011)	Eur J Radiol	EDDA	346	8	11 (4.7–19.2)	76	2	b
de Hoop et al (2010)	Radiology	Riverain Onguard 5.0	111	6	12.0 (5.1–50.7)	61	2.4	ns
Meziane et al (2010)	AJR Am J Roentgenol	Riverain Onguard 3.0	200	18	16.9	63	3.3	ns

Abbreviations: AJR Am J Roentgenol; AJR. American journal of roentgenology; CAD, computer-aided detection; Eur J Radiol, European journal of radiology; FP, false positive; J Thorac Imaging, Journal of thoracic imaging; KJR, Korean journal of radiology; N/A, not available; ns, nonsignificant.
Note: Riverain Onguard (Riverain Technologies, Miamisburg, OH); EDDA (EDDA Technology, Inc., Princeton, NJ).
[a]$p < 0.01$.
[b]$p < 0.05$.

of potential lung cancer when aided by the computer,[44,54–59] also several studies reported no increase in the performance (►**Table 2**).[60–63] The main issue that is highlighted in these articles is that it is very difficult to discriminate between true positive- and FP CAD marks. When a system produces many FP CAD marks, it is likely that a substantial number of these FPs gets accepted, potentially resulting in overdiagnosis and overtreatment to the patient. With a decline in FP CAD marks in the latest studies, improvement is more easily achieved.

To improve performance of the CAD system, bone suppressed images or dual energy acquired images can be used. Since many FPs are generated by overprojections of bony structures, inclusion of these images could improve CAD performance.[64,65] Usage of either digital bone suppression or dual energy images does not seem to make a lot of difference.[66] However, indifferent results were seen when radiologists were offered the combination of bone suppression and CAD for the detection of pulmonary nodules.[67,68]

Not only for pulmonary nodules, but also for the detection of other disease, CAD in chest radiography starts to play a role. Software algorithms for the detection of TB have been developed for application in high burden countries. Expertise of readers in high burden countries is often poor. Since CXR is a powerful TB screening instrument, research has focused on automated detection of TB in CXRs. Background of different TB detection techniques are discussed in the studies by Arzhaeva et al and Ginneken et al.[69,70] TB can have multiple different characteristics on CXRs. Therefore, these detection applications do often not only focus only on focal lesions, but also try to qualify an image as normal or abnormal based on multiple factors. The latest developed software achieves performance comparable to clinical officers in Zambia, and therefore could be used as point-of-care decision tool to select subjects that should undergo further tests.[71]

For ILD computerized detection started more than 20 years ago, with many approaches.[72–74] Automated detection of ILD was found to be extremely challenging. Since interstitial disease presents itself with diffuse patterns, software algorithms focus on specific texture analysis. The main approach is to detect the various patterns, in which ILD can be present. Abnormality scores generated by the system can be based on local areas or a more global approach where the whole image is given one score. Another complicating factor is the large amount of anatomical structures occluding the interstitial patterns. Therefore, CAD approaches for texture analysis could benefit from inclusion of digitally bone suppressed images or dual energy acquired images.[75,76]

Other research focuses on the computerized detection of emphysema in chest radiographs,[77,78] detection of pneumothorax,[79] and the automatic detection of catheters and tubes.[80–82] Also CAD software for the detection of vertebral compression fractures on lateral examinations has been developed.[56]

Currently there are two U.S. Food and Drug Administration (FDA) approved CAD systems (IQQA-chest, EDDA Technology, Inc., Princeton Junction, NJ; ClearRead + Detect, Riverain Technologies, Miamisburg, OH) for the detection of lung nodules on the market. Besides these commercial systems there are also multiple prototypes used for research purposes in various hospitals around the world. Other developed CAD systems for the detection of TB, ILD, emphysema, pneumothorax, catheters, and tubes or vertebral fractures are not yet being used in clinical practice.

Temporal Subtraction

An important part of the evaluation of a chest radiograph is based on the comparison with previous radiographs. Since nowadays all the images are digitally stored in a digital archive system, temporal subtraction has become technically feasible and attractive. Temporal subtraction is aimed to enhance the changes over time. This refers to new lesions

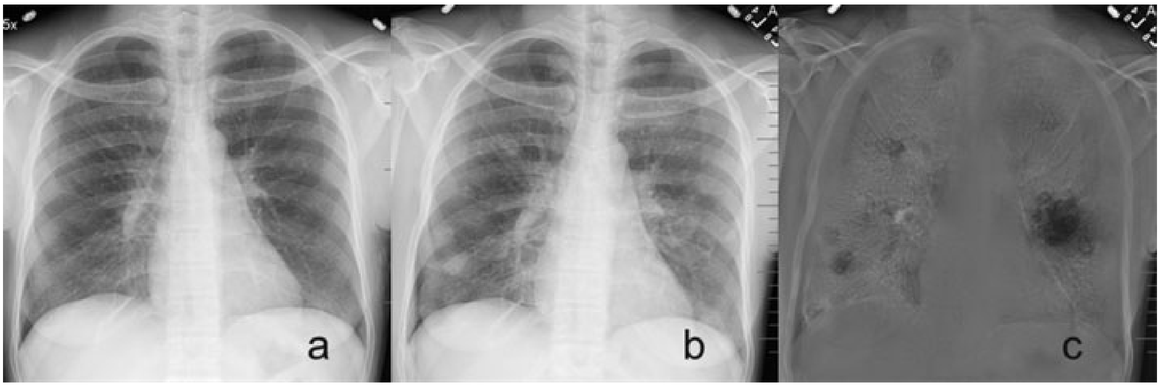

Fig. 11 Previous radiograph (a) is registered to the current radiograph (b) and subtracted to generate a subtraction image (c) (Riverain Technologies, Miamisburg, OH). Bone suppressed images are used to improve the subtraction image. The subtraction image clearly reveals newly formed focal lesions in the left and right lung, while only minor misregistration artifacts of the ribs can be seen.

as well as to the assessment of progression or regression of pathology over time.

With temporal subtraction a previous image is registered to the current image, using registration algorithms to warp the position of the previous radiograph to the current radiograph. If the registration is successful and the image is subtracted, an interval change stands out as a dark or bright area in the radiograph. One major benefit of temporal subtraction is that it is able to totally rule out the background anatomical noise. If the registration is perfect, solely interval changes thus potential pathology are highlighted.

Although temporal subtraction was already discussed in 1976,[83] reasonable attempts to automatically subtract radiographs started in 1994 by the University of Chicago.[84] Registration mismatch is responsible for most of the artifacts and represent the crucial challenge. Depth of inspiration, positioning, and rotation of the patient, makes registration of chest radiographs very difficult. In one of the early studies, where a consecutive set of cases was analyzed, 81% of the subtraction images were of clinically acceptable quality.[85] As the ribs are very radiopaque, mismatch of the ribs causes the most pronounced artifacts. Usage of dual energy subtracted or bone suppressed images, could reduce this effect,[86] which is why developers are now using a combination of bone suppression and temporal subtraction (►**Fig. 11**).

Several studies tested the effect of temporal subtraction images on the detection performance of various abnormalities. Difazio et al[87] found significant improvement in a study with 50 chest radiographs, including 29 lungs with abnormalities such as new opacities and lung nodules. Eleven radiologists significantly improved their performance when using temporal subtraction images in addition to the current and previous radiograph. Later studies confirmed these results in studies with radiographs containing pulmonary metastasis,[88] hazy pulmonary opacities including interstitial disease patterns,[89,90] and lung nodules.[91–93] Not only detection performance could be improved, also reading time of CXRs reduced significantly,[87] and was more pronounced in cases without registration mismatch artifacts.[94] The latest available commercial software package includes bone suppressed images in the temporal subtraction process. In their FDA approval study they found a significant increase in the detection of lung nodules in a study with 422 pairs of radiographs and 15 radiologists.[95] Also, recently temporal subtraction images are being used to improve CAD systems.[96]

Up to now, only in Japan temporal subtraction is fully integrated in daily clinical practice. Commercial available systems are Truedia/XR (Mitsubishi Space Software Co., Ltd., Tokyo, Japan) and Compare (Riverain Technologies). Mismatch artifacts is the biggest cause why temporal subtraction has not been adapted into clinical practice.

Summary

The two major detector systems widely applied for digital radiography are CR systems based on storage phosphor plates and solid-state (flat panel) DR systems.

CR represents the older system, matured over decades with some important recent improvements with respect to dose efficiency and workflow efficiency that strengthened its position. It represents a very versatile medium, economically attractive system that is equally suited for integrated systems as well as for cassette-based imaging at the bedside.

DR systems offer superb image quality and realistic options for dose reduction based on their high dose efficiency. While for a long time only integrated systems were available suited for a large patient throughput, also mobile DR systems became recently available.

While for the next years, it is likely that DR and CR systems will coexist, the long term perspective of CR will depend on innovations with respect to dose efficiency and signal-to-noise characteristics while for DR economic aspects and broader availability of mobile systems will play a role.

Advanced processing techniques have become available for clinical use in the last decade. Dual-energy radiography, digital bone subtraction, tomosynthesis, temporal subtraction, and CAD have been shown to considerably increase detectability of focal lesions in radiography, that way strengthening the role of radiography compared with 3D acquisition techniques such as CT. Although, many of the above mentioned techniques are not yet commonly used in clinical practice, many of them show an improved discernibility of pathology in chest radiographs. It seems to be a matter of time until certain advanced processing techniques are being adapted to standard clinical care. Digital software solutions seem to have advantages over hardware solutions, since those can easily be incorporated in the radiology department, and are often much cheaper.

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