Two-dimensional mammography is widely used in clinical environments for early detection and diagnosis of breast cancer. In recent years, tomosynthesis has been used as a new method for breast-cancer examinations. At Fujifilm, to achieve an optimal testing performance in the diagnosis and screening of breast cancer, we developed "AMULET Innovality," a mammography device comprising tomosynthesis imaging-modes with two different exposure angles. Clinical examinations performed by multiple physicians qualified as mammography instructors in Japan verified that each mode exhibited an effective testing performance. Furthermore, this newly developed technology will reduce doses of radiation via the addition of tomosynthesis.

Abstract

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1. Introduction

Tomosynthesis is coming into use across the world as studies are indicating its efficacy in breast cancer examination. Tomosynthesis captures images of a subject at different angles and produces a slice image reconstructed from those images. Tomosynthesis is expected to improve breast cancer examination. For instance, unlike the conventional mammography, a tumor or any other lesion is shown separately from mammary glands and a lesion hard to detect in the conventional method is more easily detected. In the US, this technology is already used for screening. In many other countries, the technology is used on a trial basis to verify the efficacy in screening. The use of the technology is also spreading for the purpose of diagnosis.

This paper provides an overview of technologies used for the AMULET Innovality, such as our original tomosynthesis technology, Flat Panel Detector (FPD) for imaging, Auto Exposure Control (AEC) and new image processing technology.

1.1 Principle and features of tomosynthesis

Tomosynthesis produces (reconstruct) a slice image of an area in breast by capturing images of compressed and fixed breast at different angles and synthesizing those images (projection images). As slice images at different depths are produced, a lesion overlapped in the depth direction (compressed thickness direction) by mammary glands or other parts can be observed separately from those parts. Fig. 1 shows schematic diagrams of tomosynthesis and slice images. As areas overlapped in the thickness direction are separated, a lesion with low contrast, difficult to detect in the conventional mammography, is detected more easily and 3D configuration of calcification is identified easily.

Unlike CT scanning 360 degrees of a subject, tomosynthesis scans breast in the same positioning (compressing) as that of the conventional mammography with the detector fixed. Images are captured within a limited range of angles, such as 15 degrees and 40 degrees. Overlapped areas cannot be separated as clearly as CT. However, the spatial resolution is high and the nature of a lesion is imaged more in detail.
2. Features of tomosynthesis of AMULET Innovality

Tomosynthesis of the AMULET Innovality is equipped with our original technologies focused on quality images. For instance, it is provided with two imaging modes (exposure angle and image pattern) optimized for purposes (diagnosis or screening) to maximize the examination performance.

2.1 Two tomosynthesis modes assuming examination situations

In mammographic examination, it is important to provide clear images of the characteristics of a lesion or a tissue and clarify their positional relationship with surrounding tissues. Those enhance the detection capability and increase the reliability of diagnosis. They are also extremely useful in that they provide advance information for an ultrasound examination or a biopsy.

In tomosynthesis, the larger the exposure angle is the higher the resolution in the depth direction (Z-resolution) becomes, and a lesion can be imaged separately more clearly from overlapping mammary glands and its structure is shown more in detail. Increasing the exposure angle, however, has several disadvantages. For example, it increases the travel distance of X-ray tube and that increases the exposure time and the burden on the examinee. The angle of incidence of X-rays becomes steeper and that narrows the range of areas to be reconstructed into an image. Tomosynthesis of the AMULET Innovality has two modes (exposure angles and Z-resolutions are shown in Fig. 2) to allow the user to make the optimum choice for the purpose of use and required image quality. In the HR mode, the exposure angle is set to ±20° to maximize the Z-resolution, considering exposure time and image range. The ST mode is designed for high speed exposure. The exposure angle is set to ±7.5°.

The pixel size, which determines the resolution in a slice image, is designed based on purpose and required image quality. In the HR mode, small pixels are desirable to maximize the visibility of the shape of a small structure, such as calcification and an margin of tumor mass, as the use for diagnosis is assumed. If the pixel size is reduced, the reachable dose per pixel decreases and the graininess declines due to X-ray quantum noise. In addition, the exposure angle in the HR mode is large and thus the effective breast thickness is increased and the dose reaching the detector is reduced. To strike a balance between those factors, the pixel size for reconstruction in the HR mode is set to 100 um/pixel. In the ST mode, large pixels are desirable as the use for screening is assumed and the mode must support high-speed low-dose imaging. If the pixel size is increased, the visibility of the shape of a lesion is reduced. Considering those factors, the pixel size for reconstruction in the ST mode is set to 150 um/pixel.

In both modes, the image processing is optimized based on each Z-resolution. Structures that appear on the plane of focus differ between the HR mode and the ST mode due to the difference in Z-resolution. To make the images similar to the conventional mammographic images, the degree of emphasis on a focused structure on the plane is optimized.

2.2 Two image patterns appropriate to image reading style

Some users require similar image quality to that of the conventional mammography. Other users require a clearer view of a fine structure in breast. To meet both needs, tomosynthesis of the AMULET Innovality conducts two types of image reconstruction with the conventional mammographic image quality and CT image quality. Fig. 3 shows the conventional mammographic image, an image similar to conventional mammographic quality (Pattern 1) and an image similar to CT imaging (Pattern 2). Pattern 1 is reconstructed with natural density information, similar to the conventional mammographic image, using an improved ramp filter that allows low-frequency wave to pass through and relatively emphasizing low frequency. Pattern 2 is reconstructed to clearly show fine and linear structures, including calcification and spicula formation, using a filter based...
on a ramp filter commonly used for CT and relatively emphasizing high frequency.

Tomosynthesis of the AMULET Innovaity allows selection of those two types of image reconstruction by simple operation.

2.3  Our original image reconstruction with artifact suppression

As reconstruction for tomosynthesis, just as CT, the filtered back projection (FBP) and the iterative reconstruction are used. Compared with the FBP, the iterative reconstruction enables reduction of artifacts, such as those in the shape of black belt around calcification or other high absorption matter and ripples, overlaps of structures on different planes of focus. Many researchers are studying this process. The iterative reconstruction, however, requires a huge volume of calculations and it takes too long to display an image.

The AMULET Innovaity provides our newly developed original reconstruction that has the sharp imaging and noise characteristics of the FPD, a direct converting method, while minimizing artifacts. As shown in Fig. 4, in the image reconstructed by our original process, black belt artifacts are not generated even in an area where contrast between slice images is large. That is made possible by frequency filtering. Also, the calculation time is minimized by parallelizing image reconstruction and image processing using the GPU (graphics processing unit: A dedicated integrated circuit for image processing calculations) (Table 2).

2.4  Z-resolution of tomosynthesis

Table 1 shows the Z-resolutions of tomosynthesis of the AMULET Innovaity. In accordance with the Z-resolution measurement method specified by the European Reference Organisation for Quality Assured Breast Screening and Diagnostic Services (EUREF), we have measured difference between the averages of the pixel values of the aluminum ball and the peripheral pixel values in the reconstructed image and measured the full width at half modulation (FWHM) as the Z-resolution.

2.5  System design that minimizes exposure time

Minimizing the exposure time is much needed. If the exposure time is long, the burden on an examinee is increased as the breast has to be compressed for a long time. Also, an examinee is likely to move and that blurs the image.

Tomoynthesis imaging time of the AMULET Innovaity in both modes is minimized, thanks to the high-output X-ray radiation, high-speed image reading and the optimum design of balancing the operation speed and safety of the X-ray tube (Table 2). An image is displayed promptly after the end of exposure and the positioning can be checked early.
3. X-ray imaging and exposure technology of the AMULET Innovality

Besides tomosynthesis, our new original technologies are used for the direct conversion detector and the AEC to enhance the quality of mammographic examinations with the AMULET Innovality (Fig. 5).

3.1 FPD with HCP structure that enables low dose exposure

A direct conversion system using amorphous selenium (a-Se) is used for the AMULET Innovality to meet the needs of resolution high enough to detect slight calcification. Also, the TFT image reading is employed to capture several images continuously in a short time.

The conventional direct conversion TFT system has a drawback. If the pixel size is reduced for high definition, the collection efficiency of signal charges generated by X-rays (sensitivity) is reduced. The AMULET Innovality balances high definition and high sensitivity, using our original pixel electrode shape.

In the conventional direct conversion TFT system, a signal wire and a scan wire are laid between the charge collection electrodes. In the area between the electrodes, the electric field intensity is decreased and that reduces the charge collection efficiency. We have analyzed a sharp drop in the field intensity in a gap between the opposing corners of two pixel electrodes using the conventional structure. We have developed our original hexagonal close pattern (HCP) structure which can have a wider corner angle of each electrode than the square pixel structure in the conventional TFT system and minimize the gap between pixels and found that the HCP structure suppresses a drop in the field intensity most efficiently and increases the efficiency in collecting charges. As shown in Fig. 6, the HCP structure, compared with the square pixel structure, keeps high field intensity in a gap between the opposing corners of pixels where the field intensity is liable to drop. The sensitivity is improved by 20% from that of the square pixel structure\(^1\)\(^0\).

3.2 Image quality of FPD with HCP structure

We have compared the image quality of the AMULET Innovality equipped with the HCP structure FPD with that of the AMULET equipped with the square pixel structure FPD. We have measures MTF and DQE as indices of image quality in accordance with the IEC62220-1-2\(^1\)\(^0\).

Fig. 7 shows the measurement result of MTF. The spatial resolution of the AMULET Innovality is high and almost the same as that of the AMULET. Fig. 8 shows the measurement result of DQE’s frequency dependence. The DQE of
the AMULET Innovality at 0 cycles/mm is improved by 1.3 times that of the AMULET. Fig. 9 shows the measurement result of DQE’s dose dependence at 2 cycles/mm. The DQE of the AMULET Innovality is improved in the whole range of doses measured compared with the conventional structure. Particularly, DQE is dramatically improved at 0.5 mR used for tomosynthesis.

The AMULET Innovality captures 15 projection images in one tomosynthesis session. Thanks to the use of the direct conversion TFT system with the HCP structure, even if the dose for each projection image is reduced to about 7% of that in the conventional mammography, noise is suppressed and thus high image quality enough for examinations as a tomosynthesis image is provided.

3.3 Intelligent AEC (i-AEC) properly controlling the dose

The conventional AEC sets the dose suitable for an area where the mammary gland density is the highest by automatically selecting an area where the incoming X-ray intensity is the highest from several photometric areas fixed in position (used to determine the dose for irradiation after the dose that has reached the FPD by pre-irradiation is measured). Using the fixed photometry areas, it is often difficult to find an area with the highest mammary gland density depending on subject or positioning. Also, if silicone is implanted in the breast, the implant area may be selected and the dose may be set to an excessively high level. In that case, AEC cannot be used.

To overcome those problems, the Intelligent AEC (i-AEC) of the AMULET Innovality automatically analyzes an image produced by pre-irradiation and selects an appropriate mammary gland area regardless of the situation of the subject and thereby ensures stable doses. As shown in Fig. 10, i-AEC selects an appropriate mammary gland area regardless of the existence of an implant or positioning and the dose is properly controlled based on the mammary glands.

**Fig. 9** Measurement results for the dose-dependence of DQE at 2 cycle/mm using AMULET Innovality (hexagonal pixel) and AMULET (50 μm square pixel) with Wrh, 28kV, Al 2-mm filter, and 5mR in (top) the conventional mammography imaging mode and (bottom) the tomosynthesis imaging mode

**Fig. 10** Photometry areas for conventional AEC (top) and i-AEC (bottom)

**Fig. 11** Clinical performance of the HR and ST modes
4. Clinical research result of the AMULET Innovality

We have verified the clinical performance of the AMULET Innovality in the three stages below upon the ethical approval of a research institute and the consent of patients. The Appendix provides a list of clinical research reports on the AMULET Innovality.

(1) We have determined provisional exposure conditions (tube voltage and dose) of the conventional mammography and tomosynthesis (HR mode and ST mode) by comparing with different standard images of excised breast tissues immediately after surgery.

(2) We have prospectively applied the provisional exposure conditions to patients to confirm the appropriateness of the exposure conditions.

(3) After the exposure conditions were confirmed, we have examined the clinical performance of the equipment quantitatively.

The following sections provide examples of clinical studies that show the efficacy of tomosynthesis images produced by the AMULET Innovality.

4.1 Effect of the addition of tomosynthesis

To clarify the clinical value provided by adding a tomosynthesis image to a mammographic image, we have compared the results of the addition of tomosynthesis images in the HR mode (exposure angle: $\pm 20^\circ$) high in image quality and resolution and the ST mode (exposure angle: $\pm 7.5^\circ$) short in exposure time and low in exposure.

The research was conducted on 157 patients with their written consent: 79 cases for the HR mode and 78 cases for the ST mode. Eight radiologists qualified as mammography supervisor in Japan read mammographic images and then read those images with tomosynthesis images added and recorded findings on lesions and malignant potential.

Fig. 11 shows the comparison result. In the HR mode, the sensitivity improved significantly from 49% to 58% ($P < 0.001$), the specificity stayed almost the same and the area under the ROC curve improved significantly from 0.750 to 0.799 ($P = 0.001$). In the ST mode, the sensitivity improved significantly from 46% to 54% ($P < 0.001$), the specificity stayed almost the same and the area under the ROC curve improved significantly from 0.750 to 0.779 ($P = 0.02$). The result shows that the addition of tomosynthesis images contributes to improvement in examination performance as it eliminates the need of additional examinations required by wrongly diagnosing a normal case as abnormal. In comparison between the HR mode and the ST mode, there is little different in sensitivity and specificity but the improvement in the HR mode is significantly great in the area under the ROC curve ($P < 0.05$).

Fig. 12 shows an example of an HR mode image of which the sensitivity improved (a cancer case difficult to diagnose with the conventional mammographic images was detected, thanks to the addition of a tomosynthesis image). Fig. 13 shows an example of an ST mode image. The HR mode is considered suitable for a thorough check-up as the Z-resolution is high and an margin of a lesion is displayed in detail. The ST mode is considered suitable for an examination in which detection of a lesion is important as the sensitivity is improved just as the HR mode and short in exposure time and low in dose.
5. New image processing technology to further improve the examination performance of tomosynthesis

The previous section indicates that the examination performance is improved by the addition of tomosynthesis images compared with an examination with the conventional mammography only. However, addition of tomosynthesis to the conventional mammography has a problem of increasing the exposure. We believe that our tomosynthesis image quality improvement technology we developed helps reduce the exposure.

5.1 Correction of the effects of radiation quality and scattered radiation on tomosynthesis image

In tomosynthesis imaging, the grid is retracted and X-rays are emitted under the higher energy conditions than the conventional mammography. In the conventional mammography, a tungsten anode, a rhodium filter and a grid are used. In tomosynthesis, a tungsten anode and an aluminum filter are used and a grid is not used. As a result, tomosynthesis images are likely to have lower contrast than mammographic images due to the effects of radiation quality and scattered radiation. Particularly, if the breast is thick, the contrast is significantly reduced. To solve the low-contrast problem of tomosynthesis images, we have developed technology for correcting the effects of radiation quality and scattered radiation.

The technology for correcting the effects of radiation quality and scattered radiation improves the contrast of both projection images in tomosynthesis and a slice image produced by reconstructing them to a similar level of the contrast of mammographic images.

Fig. 14 shows contrast between the background and a tumor-like mass in an RM1156 phantom imaged under the exposure conditions of the conventional mammography and tomosynthesis. The charts show that the technology for correcting the effects of radiation quality and scattered radiation improves the contrast of a tomosynthesis image to a similar level to that of a mammographic image.

5.2 Reconstruction technology based on super resolution and iterative processes

Tomosynthesis shows a lesion overlapped by mammary glands separately and thus provides useful information. However, compared with the conventional mammography, it has some disadvantages. They are an increase in exposure dose, appearance of a structure on a plane other than the plane of focus and a decline in the sharpness of an image. To overcome those disadvantages, we have developed three main element technologies.

A first is technology for improving the graininess in low-dose imaging. If the dose is lower, fewer X-rays reach the detector and relatively the quantum noise increases. Signals are interrupted by noise and the image becomes hard to read. The technology improves graininess by extracting noise components that have no structure and reducing them during reconstruction.
A second is technology for suppressing structures other than those on the plane of focus. Considering that the projection angle is limited in tomosynthesis, we have optimized the coordinate calculation necessary for the projection process to drastically shorten the calculation time. In addition, massively parallel arithmetic using GPU helps achieve practical calculation time.

A third is technology for reproducing a fine structure to prevent a decline in sharpness. Super resolution technology is applied to reconstruction to improve the visibility of fine structures such as calcification and mammary glands.

Fig. 15 shows comparative measurement results between images of CDMAM phantom reconstructed by the conventional reconstruction technology and reconstructed by the newly developed technology after imaging with the dose reduced by about 40%. The curve of the conventional reconstruction technology almost coincides with the curve of the newly developed technology with low dose imaging. That shows the newly developed technology is not inferior in detection performance.

About new tomosynthesis reconstruction (Iterative Super-resolution Reconstruction: ISR) developed using those element technologies and its clinical effects, we will report on another occasion.

6. Conclusion

We have explained in technical and clinical aspects that the two tomosynthesis modes of the AMULET Innovality, different in exposure angle, are useful for breast cancer diagnosis and screening. Those processes are based on our newly developed original X-ray imaging technology. In addition, we have introduced it is possible that examination performance is improved and required dose is reduced by the technology for correcting the effects of radiation quality and scattered radiation of tomosynthesis images and the reconstruction technology based on super resolution and iterative processes. We hope that the AMULET Innovality will help enhance the performance and accuracy of breast cancer examination and we will make continued efforts to improve the diagnosis technology further.

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**Appendix of clinical studies on AMULET Innovality**

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<td>Clinical evaluation of the dual mode Tomosynthesis with newly developed FPD and image processing for Tomosynthesis</td>
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<td>2</td>
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<td>7</td>
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