Learning objectives

Different diagnostic imaging technologies, consolidated and emerging, can nowadays be applied to breast district: Mammography [1], Breast Tomosynthesis [2], Ductography [3], Magnetic Resonance Imaging (MRI) dedicated to breast [4], Automated Breast Ultrasound Systems (ABUS) with the patient in supine [5] or prone position [6] and Molecular Breast Imaging (MBI) [7].

Free-hand Ultrasound (US) plays an important role in breast diagnostics as a real-time examination, not ionizing and non-invasive, cost effective, ideal also for repetitive follow-up and able to give information about anatomy (B-Mode modality), hemodynamics (Color, Power and Pulsed Wave Doppler) [8, 9] and tissue stiffness (Elastosonography [10]). Once a suspected finding is detected in a breast, core biopsy represents a valid alternative to open surgical biopsy in order to remove the suspicious tissue [11].

Only some of the above mentioned imaging technologies are able to offer a guide (direct or indirect; real-time or as a post guiding tool) for core biopsies. The mostly used imaging technologies for breast biopsy guidance are the stereotactic (based on X-Ray) and the US [12]. Also the MRI can be used [13].

The stereotactic biopsy enables the visualization of the breast micro-calcifications (invisible to the US except when using particular technologies not well diffused or clinically validated as the twinkling artifact [14, 15](Fig. 1), and it represents the perfect choice for core biopsies related to the sampling of this kind of breast findings.

Anyway, the stereotactic breast core biopsy has limitations: it's not a real-time imaging biopsy procedure and it needs multiple scanning views, with the consequent increase of the ionizing radiation dose to the patient. Moreover, the stereotactic table makes the axilla region not to be imaged and therefore no biopsy guidance is possible in this body area. On the contrary, free hand US has the possibility to image also the axilla area and to guide biopsies in that area [16].

As per the design of the stereotactic table, some ergonomic problems can arise depending on the particular patient's conformation and the general health conditions [17]. MRI guided core biopsy is increasing due to raised availability of breast MRI systems. The advantages, with respect to US, are especially related to the high quality anatomical details provided and the large field of view (covering also both breasts at the same time). However, the MRI biopsy guidance procedures are not real-time but they are time consuming and more expensive than the US and not ergonomically optimized; in practice they are executed only when the lesion is not visible with other imaging modalities [18]. Moreover, the lesions near the chest wall, high in the axilla, or those located in the distal breast region may be better guided by US, with respect to MRI [19].

The present work describes the innovative 3D Panoramic (3DPan) tool of Virtual Navigator technology for the real-time fusion imaging of breast 3D US volumes with bidimensional (2D) US scans. This tool was used for the planning and execution of core biopsies in vivo. Furthermore, the procedure was enhanced by a Motion Compensation
(MC) technique, using a Motion Control Sensor (MCS), which corrected possible subject's voluntary, or involuntary (e.g. respiratory) movements, for patient's and sonographer's increased comfort and easier US scanning. Additional tests regarding 3DPan imaging capabilities, their practical use and usefulness for core biopsy guidance in ex-vivo will be presented as well.

**Images for this section:**

![Figure 1: Twinkling Artifact of Breast micro-calcifications, obtained with proper Color Doppler settings.](image)

**Fig. 1:** Twinkling Artifact of Breast micro-calcifications, obtained with proper Color Doppler settings.
Background

A. Subject Predisposition
For ex-vivo Virtual Biopsy and fusion imaging tests, two hand-made phantoms, one prepared with a chicken-breast and an olive with pit, and another one prepared with four olives with pit, were used. The chicken-breast wanted to be a human breast tissue simulator, while the olives with pit wanted to be solid breast mass simulators. On the ex vivo phantoms, both Virtual Biopsy and fusion imaging with 3DPan and 2D acquisitions were performed.

For in vivo real-time biopsy US Virtual Navigator guidance, 20 female patients with suspected breast lesions or for their follow-up (mean age = 36, range = 22-49) underwent US examination and core biopsy. The following core biopsy tools were used: BARD Magnum 15mm 14 gauge (Bard Biopsy Systems, Tempe, AZ, USA) on 6 patients, Hologic ATEC 12cm 9 Gauge with Suros Hologic suction unit (Hologic, Inc. Breast Biopsy Solutions, Indianapolis, IN, USA) on 3 patients and Hospital Service Spring Biopsy needle PRECISA (Hospital Service, Aprilia (Latina), Italy) on 11 patients, after signing a written informed consent (all the patients were already scheduled for breast core biopsy). The subject was lying on the examination bed, placing her arms above and behind her head, in order to keep the breast as stable as possible and in order to easily reach the axilla for examination. Fusion imaging between 3DPan acquisitions and 2D US scans was performed on 5 patients.

Tests were performed by 4 sonographers: 2 expert radiologists with 20 years of experience in breast imaging and 2 residents in radiology.

B. Image acquisition and biopsy guidance
For all the examinations and core biopsy US guidance, an Esaote MyLabTwice US system (Esaote S.p.A., Genova, Italy), equipped with Virtual Navigation option [20] Virtual Biopsy planning and real-time image fusion of 3D US with 2D US scans, was employed. Moreover, Esaote LA923, LA523 and LA533 Linear Array Probes (LA923 and LA523 - Operating Bandwidth: 4-13 MHz; CFM-PW Frequencies: 4.5 - 5.6 - 6.3 - 7.1 MHz; LA533 - Operating Bandwidth: 3-13 MHz; CFM-PW Frequencies: 3.6 - 4.5 - 5.6 - 6.3 - 7.1 - 8.3 MHz) with different reusable tracking brackets with sensor mounted (Esaote Virtual Navigator dedicated support for LA923 and CIVCO 639-042 for LA533 - CIVCO Medical Solutions, Kalona, Iowa, USA) were used. LA923 probe has an array width of 105 mm and it was mainly used for a fast acquisition of large volumes. LA533, 53 mm array width, was mainly used for Virtual Biopsy core needle planning and guidance, for small breast volumes acquisition and 2D US examination. Moreover, LA533 probe has a dual-possibility hand grip design, pinch grip and palmar grip (appleprobe design), in order to provide a neutral wrist position [21]. This resource represented an additional operator's comfort option during long examinations and during particularly difficult to-be-biopsied patient's breast areas. Moreover, the presence of a single tracking sensor on the probe enabled the usual probe handling in both pinch grip (Fig. 2) and palmar grip.
Virtual Navigator tracking of the core biopsy needle and the real-time fusion imaging between 3D and 2D US data on the US system was made possible by an electromagnetic tracking system, consisting of a transmitter on a fixed position, a small receiver mounted on the US probe through a dedicated support, a small receiver properly mounted on the core biopsy device and the MCS, which corrected possible subject's movements, applied on the examined target (in this case the patient's sternum). A twisting of the sensor cable and a blockage with plaster strips were made in order to maintain the MCS as much steady as possible. The transmitter, whose position is considered the origin of the reference space system and which is corrected by the data coming from the MCS, was kept steady by a proper support, while the position and the orientations of the US probe and of the core biopsy tool in the created 3D space were provided by the receiver units. The electromagnetic field source tip was oriented to point the target, the subject's breast, in order to address the highest intensity and the most homogeneous area of the created electromagnetic field on the US scanning area. The magnetic field produced by Virtual Navigator electromagnetic tracking system is stronger at the transmitter site and it fades with distance from the transmitter: the magnetic field was lower than the Earth's magnetic field at a distance of 78 cm from the transmitter, therefore the MCS movement freedom was possible within 78 cm. A non-metallic table was used to reduce as much as possible the interferences with the created electromagnetic field. The MC precision test was already performed and described in a previously published study [22]. The same electromagnetic tracking system, provided for the US probe, was used also for the core biopsy instruments tracking. The receiver support used for the tracking of the BARD Magnum 15 mm 14 gauge and for the Hospital Service Spring Biopsy needle PRECISA was a CIVCO VTrax Instrument Navigator (CIVCO Medical Solutions, Kalona, Iowa, USA). For the Hologic ATEC 12 cm 9 Gauge with Suros Hologic suction unit a disposable CIVCO 653-002, Sterile ATEC vacuum-assisted breast biopsy tracking bracket was used (CIVCO Medical Solutions, Kalona, Iowa, USA).

In the ex vivo tests, the needle tracking was obtained using the CIVCO eTrax Needle Tip Tracking System (CIVCO Medical Solutions, Kalona, Iowa, USA). See Fig. 3.

All the subjects were anesthetized by a sovra-pectoral approach.

C. 3DPan, Fusion Imaging Procedure and Core Biopsy execution

Before starting the Virtual Biopsy and 3DPan procedures, a check of the accuracy of the electromagnetic field was performed: the same point coordinates were measured twice in two different spatial orientations by a dedicated registration pen with the electromagnetic sensor mounted in. Accuracy lower than 0.2 cm was considered acceptable.

Virtual Biopsy, enabled by the Virtual Navigator technology, gave to the operator the possibility to plan the core biopsy needle path even before the insertion of the tool. The core biopsy needle insertion was guided in plane and out of plane with proper graphical indications in both situations. The Virtual Biopsy was used considering the single plane 2D US scan alone or considering also the fusion between the 3DPan acquisition and the 2D Us scan, in order to enlarge the field of view and have three-dimensional view of the examined and biopsied area.
A particular visualization tool of the Virtual Biopsy, the Intelligent Positioning system, allowed to activate a sort of viewfinder at the level of the tip of the core biopsy needle, in order to help the operator to reach the desired target.

The 3DPan tool, based on the electromagnetic field positioning capabilities of Virtual Navigator technology and already employed in other clinical applications [23, 24], enabled the gluing of different 3D US breast tissue volumes and the navigation within. The operator had the possibility to use the large width array transducer (LA923) and to shift to the LA523 or LA533 probe with higher maneuverability for detailed analysis of the targets (possible lesions, suspect echographic signs, etc.) by simply changing the probe, without any re-synchronization procedure between 3D and 2D views.

A thick layer of US gel (Aquasonic 100, Parker Laboratories Inc, Fairfield, New Jersey, USA) was used to ensure a complete coupling between the transducer and the examined subject's skin, to avoid black cones and dark areas on the US image and to prevent excessive pressure on the examined area, in order not to change the breast tissue shape and position.

Custom color volumetric targets were placed on the acquired 2D scans directly or on the 3D US volume, in order to identify the areas that have to be scanned and biopsied more precisely, applying different tools for increased diagnostic confidence. For in vivo tests, patients underwent US guided core biopsies for suspicious breast lesions and also Elastosonography around the US-visible lesion, Color Doppler or Power Doppler. In ex-vivo tests, core biopsies were performed using also Elastosonography.

3DPan reconstruction and gluing algorithm of different US volumes could work using two different processes: "Preview" made a 3D global reconstruction, based only on the geometric and position information given by the probe position and orientation within the Virtual Navigator electromagnetic field, while "Auto", in addition to the information coming from the tracking system, performed a data analysis focused on tissue structure recognition, in order to find the best matching among the volumes. This could be particularly useful to compensate small movements, due to breathing and/or little tissue compression caused by the US probe during scanning. Major tissue deformation leads to a failure of the automatic gluing process.

Images for this section:
**Fig. 2:** Single Virtual Navigator electromagnetic receiver which does not affect the usual probe handling in pinch grip.
Fig. 3: A - from top to bottom the picture shows: LA533 linear array appleprobe with Virtual Navigator receiver mounted; Hologic ATEC 12 cm 9 Gauge with the disposable CIVCO 653-002, Sterile ATEC vacuum-assisted breast biopsy tracking bracket; Hospital Service Spring Biopsy needle PRECISA with CIVCO VTrax Instrument Navigator; CIVCO eTrax Needle Tip Tracking System. B - Close up of the Hologic ATEC 12 cm 9 Gauge with the disposable CIVCO 653-002, Sterile ATEC vacuum-assisted breast biopsy tracking bracket. C - Suros Hologic suction unit. D - Close up of the Hospital Service Spring Biopsy needle PRECISA with CIVCO VTrax Instrument Navigator with Virtual Navigator electromagnetic receiver connected. E - BARD Magnum 15 mm 14 gauge core biopsy tool.
Findings and procedure details

Virtual Biopsy guided core biopsy was performed both in ex vivo (chicken-breast with olives with pit as mimicking lesions) and in vivo on 20 patients already scheduled for core biopsy. On 15 patients the Virtual Biopsy was performed directly with 2D scans, on 5 patients the Virtual Biopsy was used with the fusion between the real-time 2D scan and the already acquired 3DPan volumes of the same patients. On the ex vivo phantoms, both Virtual Biopsy and fusion imaging with 3DPan and 2D acquisitions were performed. The 3DPan technology enabled a wider panoramic view of the area of intervention. A proper MCS was used in order to counteract involuntary patients movements. The MCS (used only in "in vivo" tests) was placed on the patient's sternum and there fixed with plaster strips. The patients and the chicken-breast phantoms (CBP) were positioned on a non-metallic table (due to reduce any possible interference for the Virtual Navigator electromagnetic reference space).

A. Ex vivo test

The ex-vivo performance tests of the Virtual Biopsy tool were performed on the CBP with an olive (with pit) as lesion-like target (LLT). Two CBP were created: one with a single LLT and another CBP with four different LLTs. Both 2D B-Mode scans and 3DPan (B-Mode only) of the CBP were acquired with custom color volumetric targets, in order to better identify the interesting areas.

Regarding the 3DPan US, each CBP was scanned longitudinally, acquiring three US volumes (22 seconds scan time for each US 3D acquisition). The acquired US volumes were then fused together with 3DPan tool, in order to obtain a panoramic volume of almost half CBP containing the LLT. The obtained Pan volume was achieved with the "Auto" gluing algorithm. A surface shift after the US volumes gluing was noted: the reason of this shift can be found in the pressure applied on the probe during the CBP volume acquisitions. Different tissue densities of the CBP areas can lead to different compressions during scanning. The Auto gluing algorithm, recognizing and matching the inner structures of the scanned volumes (focused on the re-alignment of inner structures) and leaving a discontinuity reconstruction only at the surface level, considered the "less interesting" part of the reconstructed volume.

The LLT and its surrounding tissues were examined also using elastosonography; tissue stiffness evaluation and the relative stiffness measurements (ElaXto Ratio) were performed on the LLT and the surrounding CBP areas. In terms of elasticity, the olive, with respect to the surrounding chicken-breast, resulted 7 times harder, as measured with the ElaXto Ratio, where two Z-zones (Z1 and Z2) were traced on the ElaXto image and then the system provided a strain ratio, related to the tissues included in the traced Z-zones. The resulting value is directly proportional to the tissue elasticity included in zone Z2, compared to the one of zone Z1. The elastosonography evaluation of the LLT and the surrounding structures of the CBP stiffness was performed also during...
real-time simultaneous visualization of 2D US scan, fused with the glued volume US. Elastosonography helped the operator to clearly detect the LLT, being stiffer than the CBP surrounding tissues. Bi-dimensional US elastosonography examination was performed in different directions, scanning the CBP on several planes containing different LLT views, in order to include the whole area around the LLT.

Once the 3DPan volumes were acquired, the 2D scans were fused in real-time with the panoramic vision of the CBP area containing the LLT which was sampled using the CIVCO eTRAX Needle Guidance System.

The biopsy was planned and executed using the Virtual Biopsy tool both on the 2D scan alone and also on the 3DPan fusion when pre-acquired. Needle insertions were performed in plane and out of plane: proper graphical indications of the correct or incorrect trajectory of the needle were given to the operator in real-time (Fig. 4). In our tests, once the planning path and insertion point were decided, the operator switched off the US reference image inserting the needle, following only the Virtual Biopsy graphical indications (the system gives to the operator also the information of the distance from the target of the needle tip in cm). See Fig. 5. The US reference image was switched-on again only when the target was hit, according to the Virtual Biopsy graphical indications (Fig. 6). After the biopsy procedure, the CBP was cut in close proximity of the LLT, paying attention not to move the LLT itself and observing if the target was hit in the center as expected (Fig. 7).

The same test was performed also on a CBP with 4 LLTs. The insertion of the needle was performed also out of plane (Fig. 8) and with the real-time fusion of the pre-acquired 3DPan of the CBP area containing the LLT to be biopsied (Fig. 9). Elastosonography was used in order to check the elasticity of the tissues around the LLT (Fig. 10). After the needle insertion (also in this case performed with the US reference image switched-off), the CBP was cut in order to directly check if the target was hit in the center (Fig. 11).

B. In Vivo test
In vivo core biopsies were performed with BARD Magnum 15mm 14 gauge and with Hospital Service Spring Biopsy needle PRECISA. Both core biopsy tools were electromagnetically tracked within the Virtual Navigator reference space using the CIVCO VTrax. For the Hologic ATEC 12cm 9 Gauge with Suros Hologic suction unit a CIVCO 653-002, Sterile ATEC vacuum-assisted breast biopsy tracking bracket was used for its Virtual Navigator real-time tracking.

The in vivo tests were performed during routine US breast examinations, related to suspected breast lesions.

The MCS was used and positioned on the patient’s sternum in order to counteract involuntary movements. Virtual Biopsy test procedure was similar to the one for the in ex vivo tests. Core breast biopsies were performed both on 2D US scans alone and in 5 cases also through real-time fusion with previously acquired 3DPan volumes of the area to be biopsied.
Virtual Navigator 3DPan tool fused different 3D US B-Mode and/or three dimensional Color Doppler or Power Doppler volume acquisitions: in our tests only B-Mode acquisitions were performed. 3DPan tool made the fusion of two or more US volumes captured by an electromagnetic tracked free-hand acquisition; in order to ensure a visual continuity to the acquired volumes, a proper level of overlapping of one volume with the adjacent one was needed (5mm were considered sufficient).

The scanning velocity during Virtual Navigator 3DPan acquisitions didn't affect the reconstruction, as in the conventional 2D US panoramic imaging not electromagnetically tracked, where the quality and the dimension - length - of the final merged image is related to the acquisition scanning velocity. Furthermore, Virtual Navigator electromagnetic tracking technology enabled monodirectional scanning, without paying attention to the velocity of the transducer movement.

Two US volumes (15 seconds maximum scan time each) were acquired, using large width array LA923 on 3 subjects, then fused together with 3DPan tool and finally navigated with the more ergonomic LA533 without any re-synchronization procedure.

On 2 subjects the Virtual Navigator 3DPan tool was employed for the fusion of three volumes (15 seconds maximum scan time each) obtained directly with LA533 probe. The probe choice for the 3DPan volume acquisition depended on the breast dimensions, morphology and the area to be reconstructed. The reconstruction of the axilla needed a large amount of gel. Virtual Navigator 3DPan acquisitions were performed taking care to maintain an overlapping region among the different US volume acquisitions and to limit as much as possible the shadowing effect, which is due to poor probe-tissue coupling with consequent reduction in image quality, in order to obtain high quality B-Mode imaging in all the examined volumes. The scanning of the same volume from two different starting points was avoided in order not to confuse the reconstruction algorithm. This happens, for example, when conventionally scanning an elongated breast: the nipple area was imaged from bottom to top and vice versa, acquiring the same structures twice.

The complete duration of the US breast examination was increased by about 5 minutes, due to the 3DPan acquisitions.

Custom color volumetric targets, visible on both 2D US, 3DPan volume and Virtual Biopsy environment, were used in order to better identify the interesting areas. Color Doppler, Power Doppler, Pulsed Wave Doppler evaluations were performed also during real-time simultaneous visualization of 2D US scan fused with the glued volume US, in order to make a hemodynamic assessment of the lesions and of the surrounding areas. Elastosonography was used in order to recognize breast stiffer regions and to perform elasticity measurement among different tissues.

Virtual Biopsy tool was used in core biopsy procedures guiding both with 2D US scans only and, in case of the real-time fusion, with pre-acquired 3DPan volumes (Fig 12).

The acquisitions and the core biopsies were performed by the expert and by the non-expert operators.
All in vivo and ex vivo tests were successful: Virtual Biopsy enabled the correct core biopsy procedure both in ex vivo and in vivo for all the tests and both for the experts and for the novices.

Images for this section:

**Fig. 4:** Planning of the biopsy on the LLT of the CBP, Virtual Biopsy tool. Note that the needle is not inserted yet and that the system already shows the planned trajectory (yellow line) with the real-time position of the in-plane needle. A proper custom blue-colored volumetric target was positioned in the center of the LLT. The needle tip insertion point and its related path were planned in order to hit the center of the LLT (as shown by the yellow line).
**Fig. 5:** US reference image switched off. The operator performed the needle insertion in the CBP following only the Virtual Biopsy graphical indications.

**Fig. 6:** Ultrasound guided biopsy procedure on the LLT of the CBP (A). The LLT was biopsied in plane with the help of the Virtual Biopsy tool (B).
**Fig. 7:** After biopsy, the CBP was cut, paying attention not to move the LLT and/or the needle.

**Fig. 8:** Virtual Biopsy - insertion of the biopsy needle on the LLT of the CBP with an off-plane path.
Fig. 9: Virtual Biopsy plan of the needle insertion (off-plane insertion) with fusion imaging 3D Pan - 2D US of the area with the lesion to be biopsied. A proper custom blue-colored volumetric target was used for a better identification of the mass to be biopsied.
**Fig. 10:** Virtual Biopsy plan of the needle insertion (off-plane insertion) with elastography of the area with the LLT to be biopsied. Use of a proper custom blue-colored volumetric target for a better identification of the LLT to be biopsied.

**Fig. 11:** After the biopsy procedure, the CBP was cut, paying attention not to move the LLTs and/or the needle.
Fig. 12: Vacuum assisted Core Biopsy performed with the Hologic ATEC (A); biopsy procedure with Virtual Biopsy tool and a proper orange-sphere target for a better identification of the lesion to be biopsied. The Virtual Biopsy tool also offers the Intelligent Positioning viewfinder feature, which shows the spatial interaction needle-target from the target point of view: this feature is intended to help the operator (especially a novice one) in performing the biopsy, offering an innovative point of view for the needle insertion like having, virtually, the possibility to move the target to get stuck by the needle (B).
Conclusion

In this preliminary study, the Virtual Biopsy tool facilitated core biopsy needle insertion both in ex vivo and in vivo tests, especially for less experienced operators in US guided core biopsy procedures. With its graphical representation of the needle tip insertion point and the planning of the path within the area to be sampled, it represented a valuable tool for improved practical confidence. The confidence is even increased by the possibility to monitor in real time the tissue stiffness with elastosonography and the hemodynamics of the lesion and surrounding areas using Doppler technologies. Especially for novices, the Intelligent Positioning viewfinder feature enables an intuitive pointing of the target to be biopsied referring to the needle tip point of view.

The MCS enabled proper fusion imaging between the real-time 2D scans and the 3DPan volumetric acquisitions, despite patients' voluntary and involuntary movements. MCS innovative technology corrected subject's movements, in order to simultaneously increase his/her and the sonographer's comfort and to ease US scanning procedures.

Virtual Navigator 3DPan technology showed to be a reliable and easy tool that fused 3D US breast anatomical data with bi-dimensional US scans. Color Doppler, Power Doppler, Pulsed Wave Doppler and Elastosonography evaluations were performed while navigating within the 3DPan volume, in order to respectively analyze the hemodynamic and stiffness characteristics of the examined area. Virtual Navigator 3DPan tool worked in the breast and axilla areas as a sort of "target positioning system". Custom targeting of lesions and/or suspected areas allowed the operator to easily identify and spatially localize the targets, navigating within the imaging given by the 3D Panoramic view. The electromagnetically tracked free-hand acquisition enabled the operator to cover all the areas of interest. The possibility to acquire the US volumes with one large width array probe and the capability to navigate within the acquired 3D glued volume with another more ergonomic probe without any re-synchronization procedure between 3D and 2D views was a particularly appreciated feature. The extended duration of the examination time for the 3DPan acquisition was balanced by the increased level of confidence and the easier navigation within the 3D US volume for both the scanning operator and the Medical Doctor image reviewer. For all the patients involved in the in vivo tests, a satisfactory visual matching between the 3DPan volume and the relative 2D US was obtained.

Personal information

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References


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