Wire-Free Virtual Breast Localization Using Liquid Carbon Nanoparticles

Ma. Theresa Buenaflor, Ricardo Victorio Quimbo, Norman Val San Agustin

Asian Breast Center, Centuria Medical Makati, Metro Manila, Philippines

ABSTRACT

The emergence of improved multi-modal diagnostics including functional imaging has enabled the diagnosis of more nonpalpable breast lesions. Lesions diagnosed as early unifocal breast cancers are amenable to breast-conserving surgery (BCS). The precise localization of these lesions is a caveat to its complete removal along with sufficient surgical margins and the preservation of normal breast tissues.

Carbon marking is an alternative to needle wire localization that is easy to perform and simplifies the workflow of the multidisciplinary team involved in breast cancer care.

Key words: liquid carbon nanoparticles, non-wire breast localization, carbon nanoparticles suspension injection (CNSI), molecular breast imaging (MBI)

ISSN 2507-8364 (Online)
Printed in the Philippines.

Received: March 30, 2019.
Accepted: April 29, 2019.
Published online first: 13 May 2019.
https://doi.org/10.21141/PJP.2019.08

Corresponding author: Ma. Theresa S. Buenaflor, MD, FPCR
E-mail: ask.abc@asianbreastcancer.com
ORCiD: https://orcid.org/0000-0001-7257-1265

INTRODUCTION

Carbon is a naturally occurring element known since ancient times. Antoine-Laurent Lavoisier, a French chemist, proposed *carbon* in 1789 from the Latin *carbo* meaning "charcoal".[1] Carbon, likewise, is a pigment used to produce black ink, as when used in tattoos, leaving an indelible mark because it is biologically inert.[2] When a tattoo needle punctures the skin, a tiny wound is produced. The body responds to injury by signaling macrophages to address the injury and engulf or phagocytose the foreign body. In tattoo ink, the pigment particles are too large to be destroyed, hence, remain fixed or permanent.[3]

The same principle applies to using carbon as an alternative wire-free method to mark lesions in the breast. It is an FDA-approved substance that provides direct visual aid to the surgeon and pathologist. Grossly and microscopically, it points to the precise location of the lesion of interest.

Svane was the first one to utilize carbon particles suspended in an aqueous solution to preoperatively mark 56 non-palpable breast lesions. The stability of carbon over time remains one of its strengths as well as its characteristic to remain in the area where it is injected without dispersing into the surrounding tissues because it is water-insoluble.[4] This is in contradistinction to vital dyes such as toluidine blue, methylene blue, green isocyanate and India ink.[5] Although vital dyes are low cost, they need to be injected in the immediate preoperative period because they diffuse easily and present an impediment in the proper identification of the area to be removed.[6]

Xie et al., studied the bioaccumulation of carbon nanoparticle suspension injection (CNSI) among mice after intratumoral injection and found that its toxicity is low and confirmed its biosafety when it entered blood circulation.[7] In a study by Jiang et al., using carbon marking for preoperative marking of 16 cases, no allergic reaction was observed. The particle diameter size range

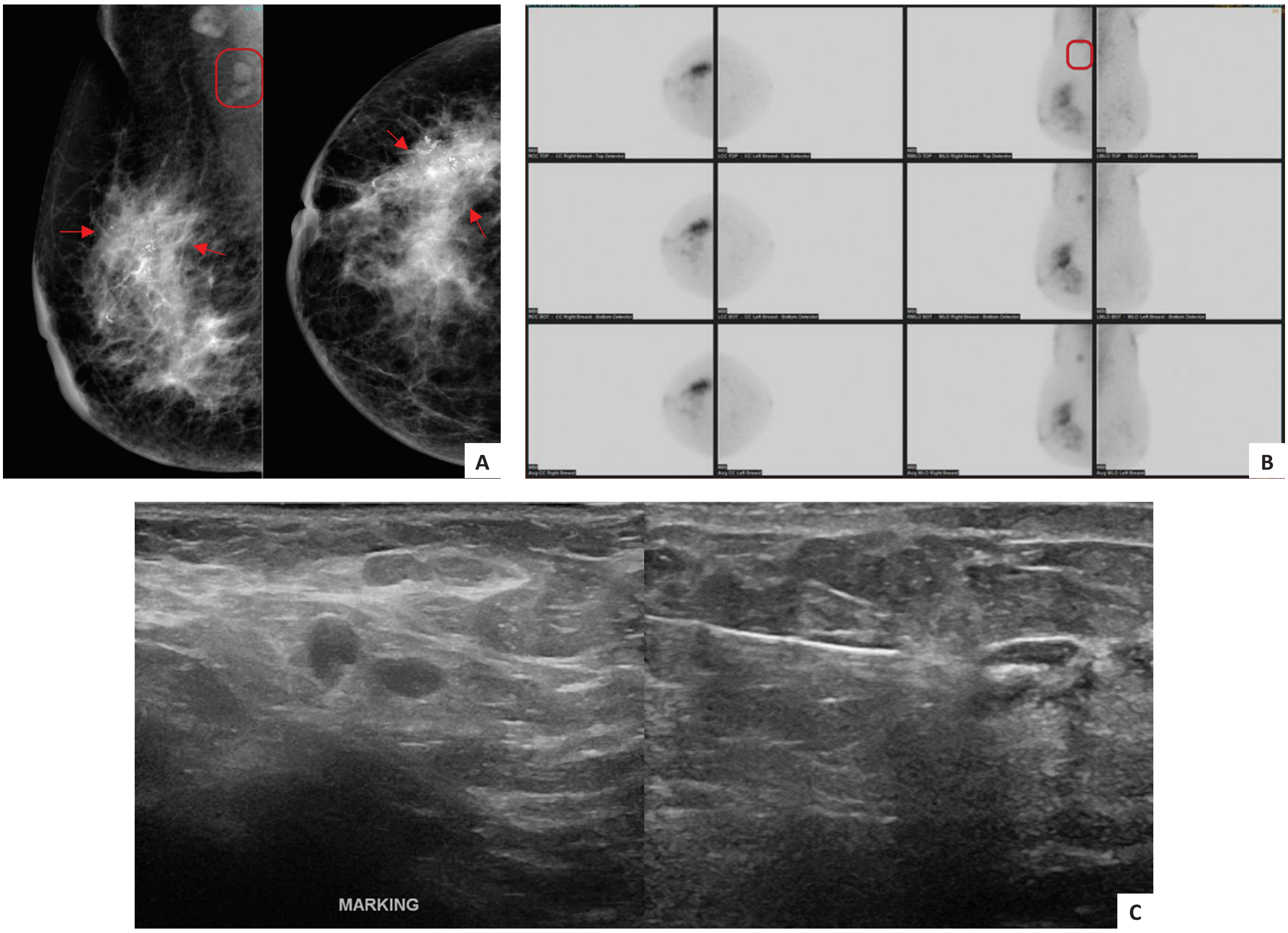

Figure 1. (A) Digital mammogram of a 65-year-old female with a palpable area at the upper outer right breast with nipple retraction and skin thickening showing heterogeneously dense breasts showing a large non-mass area of increased density with associated pleomorphic microcalcifications (marked with arrows). There are at least two hyperdense ipsilateral lymph nodes seen. **(B)** Image of Molecular Breast Imaging (MBI), a functional imaging modality using a radiopharmaceutical, 99m-Technetium sestamibi. It shows the large area of concern with marked tracer uptake (appears as black with tumor/background ratio of 11.6). The ipsilateral axilla likewise shows focus of tracer uptake with tumor/background ratio of 2.9 corresponding to the abnormal lymph node. **(C)** Correlate ultrasound image of the axilla showing the abnormal lymph node prior to and during carbon marking.

is 150-200 nm,[8,9] diluted in a saline solution and injected into the area of concern. The carbon marking can be done 10-14 days[8] before the operation and thus limit scheduling conflict.

As a method of preoperative marking, carbon localization can improve the success rate of breast-conserving surgery. Rose et al., did a head to head comparison of 219 carbon localizations and 292 hookwire localizations. Their study showed the rate of complete excision of nonpalpable lesions – with adequate surgical margins in carbon marking at 81.1% compared with wire-guided localization which is 70.8%.[10] In another study by Cavalcanti et al., 135 surgical specimens that were carbon marked showed that in all cases containing detectable lesions (98.52%), no impairment to histologic analysis was shown and the final histopathologic diagnosis was straightforward.[6]

Local experience

At our institution, carbon marking was used in 2 cases. The first case (Figures 1 and 2) involved marking the abnormal axillary lymph node prior to sentinel lymph node biopsy. The liquid carbon was injected directly into the substance of the abnormal lymph node using a Gauge 23 needle. This was to maximize the identification of the lymph node on frozen section.

The second patient (Figure 3 and 4) had carbon marking at the medial margin of the tumor to facilitate breast-conserving surgery after a 50% reduction tumor size post-neoadjuvant chemotherapy. In this case, the needle was positioned perpendicular to the probe because the direction was straight down, marking the shortest distance for the surgeon from the skin down to the lesion. Upon slow withdrawal of the needle going up, slow infiltration was done to create a track for the surgeon to follow.

The advantages of carbon marking are its ease of use and effectivity in facilitating the complete excision of nonpalpable lesions. It can withstand histological analysis and presents no diagnostic difficulty to the pathologist.[6]

Carbon marking is a valuable and accurate alternative to wire localization and has the added value of improving service delivery.

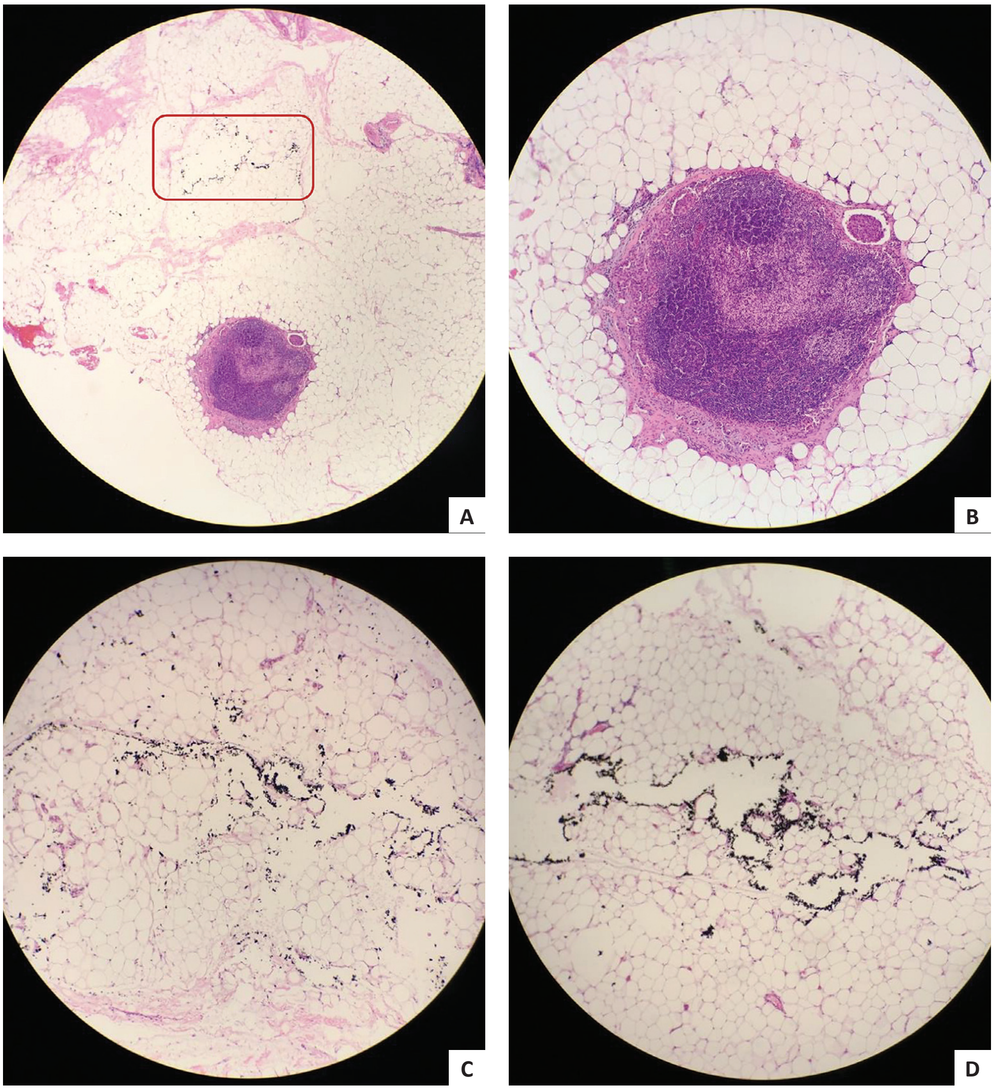

Figure 2. **(A)** Low power view of the abnormal lymph node with a 2 mm focus of micrometastasis showing black specks (red box) at the 12 o'clock position corresponding to the dye (Hematoxylin-Eosin, 10x). **(B)** High power view (Hematoxylin-Eosin, 40x). **(C, D)** Carbon nanoparticles are noted without obscuration of the cellular details (Hematoxylin-Eosin, 10x & 40x).

CONCLUSION

Preoperative marking is both a science and an art. It involves meticulous planning and precise identification of lesions. Our local experience suggests that carbon marking is a viable alternative and easily adapted method of localizing impalpable breast lesions. This technique can streamline the work of the radiologist, surgeon and pathologist.

ETHICAL CONSIDERATION

Patient consent was obtained before submission of the manuscript.

STATEMENT OF AUTHORSHIP

All authors certified fulfillment of ICMJE authorship criteria.

AUTHOR DISCLOSURE

The authors declared no conflict of interest.

FUNDING SOURCE

None.

REFERENCES

1. http://science.marshall.edu/castella/chm448/elements2.pdf [Internet]. Accessed April 29, 2019 .
2. Sperry K. Tattoos and tattooing. Part I: history and methodology. Am J Forensic Med Pathol. 1991;12(4);313-9. PMID: 1807141.
3. Wood-Black F. Going skin deep: the culture and chemistry of tattoos. Inchemistry. https://inchemistry.acs.org/content/inchemistry/en/atomic-news/tattoo-ink.html. Accessed March 18, 2019.
4. Svane G. A stereotaxic technique for preoperative marking of non-palpable breast lesions. Acta Radiol Diagn (Stockh). 1983;24(2):145-51. PMID: 6353873.
5. Patrikeos A, Wylie EJ, Bourke A, Frost F. Imaging of carbon granulomas of the breast following carbon track localization. Clin Radiol. 1998;53(11):845-8. PMID:9833790.

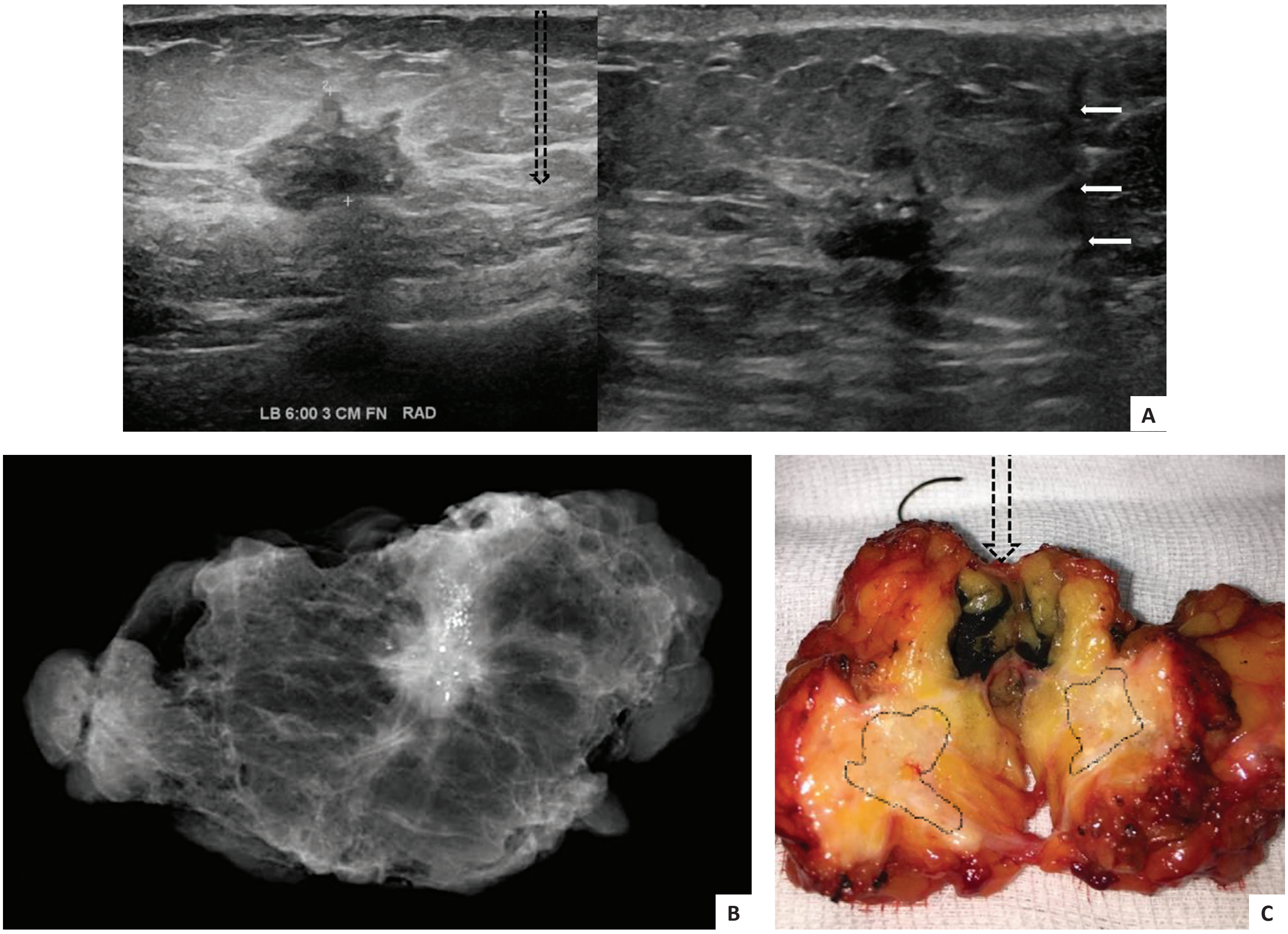

Figure 3. **(A)** A 74-year-old lady diagnosed with Invasive ductal carcinoma of the left breast post-neoadjuvant chemotherapy. With a 50% reduction in size of the mass, she became eligible for breast-conserving surgery. Ultrasound image shows an irregular markedly hypoechoic solid mass with angular margins and intralesional microcalcifications. Dotted arrow shows the area where the carbon is injected to mark the medial margin of the mass providing a visual aid to the surgeon. The thin shadowing hypoechogenicity (marked with white solid arrows) corresponds to the track of the needle. It is positioned perpendicular to the probe so that it marks the shortest distance from the skin down to the lesion. **(B)** Specimen mammogram shows the lesion located centrally. **(C)** Cut section of the gross specimen shows the irregular mass (dotted outline) and the adjacent carbon-marked area. Final histopathology showed negative margins.

6. Cavalcanti TC, Malafaia, O, Nassif, PA, et al. Non-palpable breast lesions marked with coal suspension: evaluation of anatomopathological aspects, viability of interpretation and inflammatory response. Rev Col Bras Cir. 2012:39(6):469-75. PMID: 23348642.
7. Xie P, Yang S-T, He T, Yang S, Tang XH. Bioaccumulation and toxicity of carbon nanoparticles suspension in intravenously exposed mice. Int J Mol Sci. 2017;18(12):pii:E2562. PMID: 29186019. PMCID: PMC5751165. https://doi.org/10.3390/ijms18122562.
8. Jiang Y, Lin N, Huang S, et al. Tracking nonpalpable breast cancer for breast-conserving surgery with carbon nanoparticles implication in tumor location and lymph node dissection. Medicine (Baltimore). 2015:94(10):e605. PMID: 25761181. PMCID:PMC4602461. https://doi.org/10.1097/MD.0000000000000605.
9. Ko K, Han BK, Jang KM, et al. The value of ultrasound-guided tattooing localization of nonpalpable breast lesions. Korean J Radiol 2007;8(4):295-301. PMID: 17673840. PMCID: PMC2627157. https://doi.org/10.3348/kjr.2007.8.4.295.
10. Rose A, Collins JP, Neerhut P, Bishop CV, Mann GB. Carbon localisation of impalpable breast lesions. Breast. 2003;12(4):264-9. PMID: 14659311.