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The role of breast fine needle aspiration during and post-COVID-19 pandemic: A fast and safe alternative to needle core biopsy

1 | INTRODUCTION

The coronavirus disease 2019 (COVID-19) has spread all over the world, affecting most countries to varying degrees. As of 10 July 2020, there were more than 12 million people infected worldwide and over 500 000 casualties.¹ The way the pandemic played out in certain countries, such as the first wave in Italy, have shown how taxing this virus is for healthcare systems and how dire the situation can become when they are overwhelmed.² This is true not only for those directly or indirectly affected by the viral infection. Much attention has been focused on the economical consequences of the pandemic and the measures taken to control it.³⁻⁶ However, a few reports have also focused on the consequences for those affected by other severe pathologies.^{2,7-10} Center for Disease Control data show that excess deaths, defined as the difference between observed numbers of deaths and expected numbers, excluding those attributed to COVID-19, have increased in the USA during the pandemic when compared to previous years, particularly in heavily affected areas such as the state of New York.¹¹

This may, at least in part, be attributed to the many constraints COVID-19 places on health services, both public and private. Severe cases often require access to ventilators and well-equipped intensive care units.¹² Given the insufficient capacities in many countries and hospitals, units previously used for surgical and diagnostic procedures were converted to impromptu COVID-19 units. Healthcare personnel were diverted to these units, replacing their usual duties with COVID-19 patient treatment and triage.¹³ The consequence is a reduced capacity for diagnostic and therapeutic procedures of unrelated pathologies.^{2,7-10} This capacity was further decreased by the need to adapt procedures and provide adequate personal protection equipment to healthcare professionals, since these patients may be harbouring the disease and be contagious while remaining asymptomatic.¹³ Furthermore, patients themselves may be avoiding looking for healthcare even when in need, for fear of contracting COVID-19 infection.¹⁴

Data show that this will invariably result in delays and increased waiting lists for diagnostic and therapeutic procedures of vital importance, which will be felt for years to come.^{15,16}

2 | FINE NEEDLE ASPIRATION BIOPSIES OF THE BREAST

Some of the patients affected by these delays were those with suspicious breast lesions detected clinically or through imaging studies. To recover from this situation, and reduce the increase in mortality and morbidity, innovative and unconventional strategies will necessarily have to emerge. All patients with suspicious lesions need pathological confirmation of malignancy in order to be treated, and diagnostic procedures have been deemed high priority by several international organisations.¹⁷⁻¹⁹ As already established, many of these diagnostic procedures have been delayed, resulting in procedure backlogs. Furthermore, given that recommendations have been issued to suspend imagological screening examinations of the breast, these backlogs are bound to increase as the pandemic is controlled and procedures resumed.²⁰

Current practice guidelines recommend that the diagnosis of suspicious breast lesions classified radiologically as BIRADS 4 and 5 should be made using core needle biopsies (CNBs).^{21,22} When compared to fine needle aspiration biopsies (FNABs), CNBs have some advantages, such as enabling the assessment of suspicious micro-calcifications detected by mammography, distinguishing in situ from invasive lesions and providing material for performing theragnostic biomarkers, enabling personalised therapy.²³

However, FNABs of breast lesions have a long history in western medicine, and their diagnostic value cannot be understated. When coupled with ultrasound and rapid on-site evaluation, they have been shown to be successful in the diagnosis of both palpable and non-palpable ultrasound-detectable breast lesions. Whereas CNBs are expensive, complex procedures, with an increased risk of complications, FNABs are quick to perform, cost-effective and minimally invasive.^{24,25}

In the context of the COVID-19 pandemic, these features seem advantageous. By resorting to FNABs, clinicians may be able to save time and resources, which may be very limited at this time. However, even if they are less expensive and quicker to perform, these advantages would be negated if a CNB is still needed to obtain adequate material for the confirmation of invasion or to enable ancillary testing. We would argue, however, that these problems can now, more than ever, be overcome. Firstly, ancillary tests have been shown to be viable on cytological material in the context of breast cancer, either directly performed on smears or cell-blocks.²⁶ Secondly, the International Academy of Cytology recently developed the Yokohama System for Reporting Breast Fine-Needle Aspiration Biopsy Cytopathology.²⁷ Similarly to other standardised reporting systems in cytology, the Yokohama system divides breast FNAB diagnoses into five categories, each with known and defined risks of malignancy: insufficient for diagnosis, benign, atypical, suspicious for malignancy and malignant.

The risks of malignancy and reproducibility of criteria for each of these categories have recently been validated in a meta-analysis.²⁸ In fact, looking at other organ systems such as the thyroid, these standardised systems have long enabled a successful clinical management of tumoral lesions.^{29,30} Furthermore, although a cytopathologist following the Yokohama system cannot definitively tell apart high-grade ductal in situ carcinoma from an invasive carcinoma, they should be able to differentiate these lesions from low-grade ductal in situ carcinomas and other low-risk proliferative lesions of the breast. Clinical management of high-grade ductal in situ carcinoma is very similar to the management of invasive carcinoma, allowing diagnosis and surgical management without core biopsy.²⁷ When a diagnosis of low-grade ductal in situ carcinoma is made (in the atypical or suspicious categories), a biopsy may be necessary. However, a recent series from an Italian reference centre has shown that, when performed by experienced cytopathologists following the Yokohama system, the majority of diagnoses are either benign or malignant.³¹

This would reduce the burden of CNB procedures for surgeons and radiologists alike, enabling the screening of more patients in the available time, which is of particular importance in the context of this pandemic, when resources are limited.

3 | BIOSAFETY

One could also argue that, given the minimal invasive nature of the FNAB procedure, the risk of infection from a asymptomatic COVID-19 patient should be low, and even lower when compared to a CNB procedure, which may involve more personnel and time to perform. However, biosafety hazards in cytology are not limited to the aspiration procedure itself, but also involve transport, preparation and processing of specimens such as air-dried smears. Those issues have been raised in recent publications.³²⁻³⁴

For instance, cytopathologists may work in pairs, reducing the time spent on each patient. If possible, after the procedure itself, all sample processing should be performed under a level 2 biosafety hood. However, if this is unavailable or unpractical, FFP2/N95 masks and face shields should be sufficient to adequately protect personnel. Smears can be fixed in ethanol to avoid the generation of aerosols and droplets from these samples downstream. The material obtained through the FNA procedure may also be placed in a liquid medium, such as ethanol, enabling cyto-centrifuge preparations, or

formaldehyde, enabling the preparation of cell-blocks.³²⁻³⁴ These may be prepared using one of the several methods described in the literature.³⁵

4 | CONCLUSIONS

COVID-19 is a novel virus that has taken the world by surprise, through its ease of transmissibility, asymptomatic spread and lethality. Health systems have been overburdened and struggled to cope, deferring elective diagnostic and therapeutic procedures. In the case of breast cancer, this has led to a backlog of patients, which will only worsen as imaging and diagnostic activity is resumed. CNBs of the breast have so far been the gold-standard for the diagnoses of breast lesions, given their reliability, reproducibility and accuracy of diagnosis. FNABs, however, are more cost-effective and quicker to perform. Their perceived limitations, such as the lack of a definitive diagnosis and poor interobserver reproducibility have been addressed by the Yokohama system. Furthermore, they have been shown to be able to provide adequate material for ancillary testing.

Pathologists may no longer be used to these samples, but extraordinary times require extraordinary measures. Through the use of the Yokohama system, which has been shown to be reproducible, with good communication with clinicians and image correlation, we believe that FNABs may be a valuable and even essential diagnostic tool for tumoural breast lesions in the world of COVID-19.

KEYWORDS

biosafety, breast cancer, COVID-19, cytology, fine-needle aspiration

CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

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REFERENCES

- Wordlometer COVID-19 Coronavirus Pandemic [Internet]. [cited 2020 Jul 10]. Available from https://www.worldometers.info/coron avirus/. Accessed July 10, 2020
- Kurihara H, Bisagni P, Faccincani R, Zago M. COVID-19 outbreak in Northern Italy: viewpoint of the Milan area surgical community. J Trauma Acute Care Surg. 2020;88(6):719-724.
- Palumbo LJD, Brown D. Coronavirus: a visual guide to the economic impact. BBC News [Internet]. 2020. Apr 30 [cited 2020 May 27]; Available from https://www.bbc.com/news/business-51706225
- UNIDO. Coronavirus: The Economic Impact | UNIDO [Internet]. [cited 2020 May 27]. Available from: https://www.unido.org/stori es/coronavirus-economic-impact. Accessed May 27, 2020.
- European Parliament. Covid-19's Economic Impact: €100 Billion to Keep People in Jobs | News | European Parliament [Internet]. cited 2020 May 27; 2020. Available from https://www.europarl. europa.eu/news/en/headlines/society/20200416STO77205/covid -19-s-economic-impact-EU100-billion-to-keep-people-in-jobs. Accessed May 27, 2020.
- McKinsey. Coronavirus' Business Impact: Evolving Perspective | McKinsey [Internet]. [cited 2020 May 27]. Available from https:// www.mckinsey.com/business-functions/risk/our-insights/covid -19-implications-for-business. Accessed May 27, 2020.
- Stensland KD, Morgan TM, Moinzadeh A, et al. Considerations in the triage of urologic surgeries during the COVID-19 pandemic. *Eur* Urol. 2020;77(6):663-666.
- Welt FGP, Shah PB, Aronow HD, et al. Catheterization laboratory considerations during the coronavirus (COVID-19) pandemic: from the ACC's Interventional Council and SCAI. J Am Coll Cardiol. 2020;75(18):2372-2375.
- Garcia S, Albaghdadi MS, Meraj PM, et al. Reduction in STsegment elevation cardiac catheterization laboratory activations in the United States during COVID-19 pandemic. J Am Coll Cardiol. 2020;75(22):2871-2872.
- 10. Rosenbaum L. The untold toll the pandemic's effects on patients without Covid-19. N Engl J Med. 2020;382(24):2368-2371.
- Excess Deaths Associated with COVID-19 [Internet]. 2020 [cited 2020 May 27]. Available from https://www.cdc.gov/nchs/nvss/ vsrr/covid19/excess_deaths.htm. Accessed May 27, 2020.
- Critical Care. Coronavirus Disease COVID-19. COVID-19 Treatment Guidelines. [cited 2020 May 27]. Available from https://www.covid 19treatmentguidelines.nih.gov/critical-care/. Accessed May 27, 2020.
- Peters AW, Chawla KS, Turnbull ZA. Transforming ORs into ICUs. N Engl J Med. 2020;382(19):e52.
- Dire. Unusual STEMI Complications Blamed on COVID-19 Hospital Avoidance | tctmd.com [Internet]. [cited 2020 May 27]. Available from https://www.tctmd.com/news/dire-unusual-stemi-complicati ons-blamed-covid-19-hospital-avoidance. Accessed May 27, 2020.
- The Health Foundation. Returning NHS Waiting Times to 18 Weeks for Routine Treatment [Internet]. The Health Foundation. [cited 2020 May 27]. Available from https://www.health.org.uk/ publications/long-reads/returning-nhs-waiting-times-to-18-weeks. Accessed May 27, 2020.
- Wood RM. Modelling the impact of COVID-19 on elective waiting times. J Simul. 2020;14:1-9.
- Curigliano G, Cardoso MJ, Poortmans P, et al. Recommendations for triage, prioritization and treatment of breast cancer patients during the COVID-19 pandemic. *Breast*. 2020;1(52):8-16.
- American College of Surgeons. March 24 O, 2020. COVID-19 Guidelines for Triage of Breast Cancer Patients [Internet]. American College of Surgeons. [cited 2020 May 27]. Available from https://

www.facs.org/covid-19/clinical-guidance/elective-case/breas t-cancer. Accessed May 27, 2020.

- ESMO. ESMO Management and Treatment Adapted Recommendations in the COVID-19 Era: Breast Cancer [Internet]. [cited 2020 May 27]. Available from https://www.esmo.org/guide lines/cancer-patient-management-during-the-covid-19-pandemic/ breast-cancer-in-the-covid-19-era. Accessed May 27, 2020.
- ASBrS Board of Directors and ACR Board of DirectorsASBrS and ACR Joint Statement on Breast Screening Exams During the COVID-19 Pandemic. [Internet]. [cited 2020 May 27]. Available from https://www.breastsurgeons.org/docs/news/2020-03-26-ASBrS-ACR-Joint-Statement.pdf. Accessed 27 May 2020.
- Bevers TB, Helvie M, Bonaccio E, et al. Breast cancer screening and diagnosis, version 3.2018, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2018;16(11):1362-1389.
- 22. Cardoso F, Kyriakides S, Ohno S, et al. Early breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†. *Ann Oncol.* 2019;30(8):1194-1220.
- 23. Nassar A. Core needle biopsy versus fine needle aspiration biopsy in breast—a historical perspective and opportunities in the modern era. *Diagn Cytopathol.* 2011;39(5):380-388.
- 24. Vetto J, Pommier R, Schmidt W, et al. Use of the "triple test" for palpable breast lesions yields high diagnostic accuracy and cost savings. *Am J Surg.* 1995;169(5):519-522.
- Dong J, Ly A, Arpin R, Ahmed Q, Brachtel E. Breast fine needle aspiration continues to be relevant in a large academic medical center: experience from Massachusetts General Hospital. *Breast Cancer Res Treat*. 2016;158(2):297-305.
- Beca F, Schmitt FC. Ancillary tests in breast cytology: a practical guide. Acta Cytol. 2019;63(4):302-313.
- Field AS, Raymond WA, Rickard M, et al. The International Academy of Cytology Yokohama system for reporting breast fine-needle aspiration biopsy cytopathology. ACY. 2019;63(4):257-273.
- Hoda RS, Brachtel EF. International Academy of Cytology Yokohama system for reporting breast fine-needle aspiration biopsy cytopathology: a review of predictive values and risks of malignancy. Acta Cytol. 2019;63(4):292-301.
- 29. Cibas ES, Ali SZ. The 2017 Bethesda system for reporting thyroid cytopathology. *Thyroid*. 2017;27(11):1341-1361.
- 30. Haugen BR, Alexander EK, Bible KC, et al. 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the American Thyroid Association guidelines task force on thyroid nodules and differentiated thyroid cancer. *Thyroid*. 2016;26(1):1-133.
- De Rosa F, Migliatico I, Vigliar E, et al. The continuing role of breast fine-needle aspiration biopsy after the introduction of the IAC Yokohama System For Reporting Breast Fine Needle Aspiration Biopsy Cytopathology. *Diagn Cytopathol.* 2020. 1– 10. https://doi. org/10.1002/dc.24559
- 32. Pambuccian SE. The COVID-19 pandemic: implications for the cytology laboratory. J Am Soc Cytopathol. 2020;9(3):202-211.
- Chen C-C, Chi C-Y. Biosafety in the preparation and processing of cytology specimens with potential coronavirus (COVID-19) infection: perspectives from Taiwan. *Cancer Cytopathol.* 2020;128(5):309-316.
- Vigliar E, laccarino A, Bruzzese D, Malapelle U, Bellevicine C, Troncone G. Cytology in the time of coronavirus disease (COVID-19): an Italian perspective. J Clin Pathol. 2020;2020-206614. Available from https://jcp.bmj.com/content/early/2020/04/19/ jclinpath-2020-206614.
- Rollins SD, Russel DK. Cytopathology in focus. cell blocks: getting the most from the least invasive method. Northfield, IL: CAP Today; 2017.