INFORMATION BRIEF (RAPID REVIEW)

Digital Solution for Breast Cancer Recurrence Risk Profiling and Cancer Therapy Guidance

Malaysian Health Technology Assessment Section (MaHTAS)
Medical Development Division
Ministry of Health Malaysia
025/2023

IPT Mark
Rapid Review
INAHTA

Malaysian Health Technology Assessment Section (MaHTAS)
Medical Development Division
Ministry of Health Malaysia
Level 4, Block E1, Precinct 1
Government Office Complex
62590, Putrajaya
Tel: 603 8883 1229

Available online via the official Ministry of Health Malaysia website: http://www.moh.gov.my

SUGGESTED CITATION: Ana Fizalinda AS, Izzuna MMG. Digital Solution for Breast Cancer Recurrence Risk Profiling and cancer therapy guidance. Information Brief. Ministry of Health Malaysia: Malaysian Health Technology Assessment Section (MaHTAS); 2023. 9 p. Report No.: 025/2023

DISCLOSURE: The author of this report has no competing interest in this subject and the preparation of this report is entirely funded by the Ministry of Health Malaysia.

DIGISTAIN: DIGITAL SOLUTION FOR BREAST CANCER RECURRENCE RISK PROFILING AND CANCER THERAPY GUIDANCE

PURPOSE

To provide brief information on the effectiveness, safety, and cost-effectiveness of digital solution for breast cancer recurrence risk profiling following a request from the Director General of Health Office, Ministry of Health, Malaysia.

BACKGROUND

Breast cancer (BC) treatment has evolved in the past decades due to the discovery of specific prognostic, predictive biomarkers and treatment that enable the application of more individualised therapies to patients with different molecular subgroups. These subgroups show specific differences regarding biological clinical behaviour. In addition to the classical clinical prognostic factors of breast cancer, established molecular biomarkers such as oestrogen receptor and progesterone receptor have played a significant role in the selection of patients benefiting from endocrine therapy for many years. The human epidermal growth factor receptor2 (HER2) has been validated to be not only a prognostic factor, but also a predictor of response to HER2 targeting therapy. The shift toward an earlier diagnosis of breast cancer due to improved imaging methods and screening programs highlights the need for new factors and combinations of biomarkers to quantify the residual risk of patients and to indicate the potential value of additional treatment strategies.[1]

Breast cancer (BC) is one of the most prevalent types of cancers diagnosed in women all over the world. It has been reported as the second leading cause of mortalities due to cancers in the United States in 2021.[1,2] In Malaysia, regardless of gender, breast cancer contributed to 19.0% of all new cancer cases diagnosed in 2012 - 2016 compared with 17.7% in 2007 - 2011. The new cases of breast cancer had increased from 32.1% to 34.1% of overall cancer among women in similar period of comparison which gave a 2% increment. The Age Standardised Incidence Rate (ASR) had increased to 34.1 per 100,000 populations in 2012 - 2016 from 31.1 per 100,000 populations in 2007 - 2011. The incidence started to increase at the age of 25 and peaked at the age of 60 to 64 years. The incidence was highest among Chinese (40.7 per 100,000) followed by Indian (38.1 per 100,000) and Malay (31.5 per 100.000). The overall lifetime risk was 1 in 27, with 1 in 22 for Chinese, 1 in 23 for Indians and 1 in 30 for Malays. The patients with BC are at risk of local recurrence as well as axillary lymph node metastasis despite early detection of the disease and successful surgical resection.[2] While the 5-year survival rate of BC patients at early stages is over 90%, this rate declines to <30% after the occurrence of metastasis.[1]

The [redacted]s a mid-infrared imaging technology that assesses aneuploidy by measuring the nuclear-to-cytoplasmic chemical ratio in the cellular content of tissues to generate the Digistain Index (DI). The Digistain Prognostic Score (DPS) has been developed by

incorporating DI with pathological features. The ability of DPS to predict clinical outcomes in patients with HR-positive HER2-negative primary breast cancer was investigated as a means to guide adjuvant chemotherapy. Currently, the association of the DPS with outcomes in patients with HR-positive HER2-negative breast is being tested in an ongoing trial.[3] Unlike genomic tests, Digistain® claimed as a novel tool to measures markers at the protein level using a unique combination of optical scan technology and artificial intelligence (AI). Therefore, the used of AI able to avoid the quality control and reproducibility issues common to RNA isolation from formalin-fixed tissue. [redacted]ses mid infrared spectroscopy to detect and measure chemical moieties whose concentrations are known to correlate with tumour malignancy. By performing such measurements on tumour tissue where genomic expression has already manifested morphologically, [redacted] measurements avoid the inherent challenges that exist in genomic measurement of formalin fixed tissue samples driven by variations in tissue fixation.[4] **(See Figure 1)**

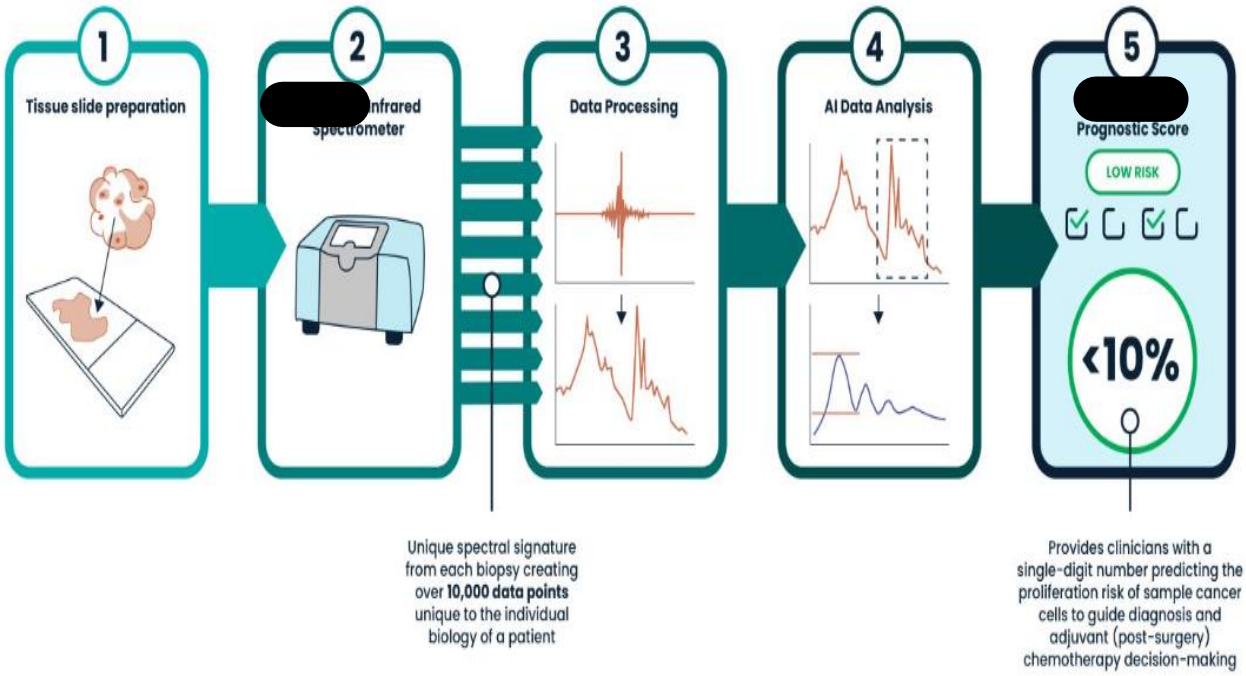

Figure 1**:** [redacted] **How it works**

The used of AI and machine learning algorithms are increasingly being applied to assist pathologists in grading cancers and predicting patient prognosis. These technologies may analyse large datasets to identify patterns and features that may not be easily discernible by the human eye. Digital solutions are integral to the advancement of precision medicine, where treatment decisions are tailored to the specific characteristics of an individual's cancer. Recently, molecular profiling and genetic analysis may contribute to a more accurate prognosis and treatment strategy.[4]

EVIDENCE SUMMARY

There was one study retrieved from the scientific databases via OVID, PubMed and general search engines (Google Scholar), using the search term; *Digistrain*, tumour profiling tests, mid-infrared spectroscopy and *breast cancer.* The last search was conducted on 25 January 2024. Apart from an extended hand search and document provided from the requestor, only a few articles identified which were an abstract and an unpublished study.

EFFICACY/ EFFECTIVENESS

A study was conducted by Coombes et al. at the University Hospital of Nottingham, United Kingdom to validate the Digistain Prognostic Score (DPS), developed by incorporating DI with clinicopathological features to predict 5- and 10-year recurrence-free survival (RFS), recurrence and overall survival (OS) among 801 patients with HR-positive HER2-negative primary operable breast cancer and ≤3 positive lymph nodes (LN). The median age at diagnosis was 53 years and median tumor size was 1.6 cm. Most patients had a ductal tumor (85.02%), while much smaller proportions had lobular tumors (10.36%) or special-type cancers (4.37%). At the time of diagnosis, 46.32% had a good NPI score (>2.4 and ⩽3.4), 46.32% had a moderate NPI score (>3.4 and⩽5.4), and 7.24% had a poor NPI score (>5.4) (with data missing for one patient). The median length of follow-up from diagnosis to last follow-up was 12.7 years (range: 0.9 to 19 years), with 90% of patients experiencing no recurrence in the 10 years from diagnosis. The patients received systemic adjuvant endocrine therapy, but no chemotherapy. The results from a Cox model showed there were significant associations (p <0.01) between OS and tumor grade (hazard ratio (HR): 1.81; 95% CI 1.46 to 2.30), tumor size (1.37; 1.19–1.57), age (1.04; 1.03–1.06), and LN stage (1.78; 1.34–2.36). As for DI the hazard ratio was 4.49 (95% CI 1.08–18.67), p = 0.039. When DI was combined with the other variables to generate the DPS, the area under the curve (AUC) values of the receiver operating curve (ROC) in the four subgroups (lymph node negative lymph node positive, age ≤50 years (premenopausal), age ≥60 years (post-menopausal) were similar for all outcomes ranging from 0.67 to 0.80 and 0.60 to 0.75 for 5 and 10 years, respectively. There were similar trends of low (<0.21) positive predictive values (PPV) and high (>0.84) negative predictive values (NPV) across all groups and clinical outcomes. In the total population, the hazard ratio for DPS was statistically significant (p< 0.001) for low- versus high-risk classification for all three clinical outcomes namely recurrence free survival, recurrence and overall survival (1.80, 1.83 and 1.77 respectively).[5]

SAFETY

There was no retrievable evidence from the medical databases on the cost/cost-effectiveness o[redacted] as digital solution for breast cancer recurrence risk profiling and cancer therapy guidance for breast cancer.

COST/COST-EFFECTIVENESS (If any)

There was no retrievable evidence from the scientific databases on the cost/cost-effectiveness of [redacted] as a digital solution for breast cancer recurrence risk profiling and cancer therapy guidance for breast cancer. The price for the device was not available, but a health economic study indicated and predicted that [redacted] can lead to a cumulative savings of an average of £286.7 million for an intermediate-risk patient population once rolled out as a substitute.[6]

CONCLUSION

Based on the review, there was limited evidence on Digistain® as a digital solution in terms of its accuracy, predictive performance, and stratifying patients with early breast cancer into low or high risk. Larger studies with longer follow-up are warranted to further establish its effectiveness, safety and cost-effectiveness.

REFERENCES

1. Weigel MT, Dowsett M. Current and emerging biomarkers in breast cancer: prognosis and prediction. Endocr Relat Cancer. 2010 Sep 23;17(4): R245-62
2. Ministry of Health Malaysia. Management of Breast Cancer (Third Edition). Putrajaya: MoH; 2019.
3. Amrania H, Coombes RC, Palmieri C, et al. 65P Association of the digistain prognostic score with outcomes in patients with HR-positive HER2-negative breast cancer. ESMO Open. 2023 May 1;8(1)
4. Dramatically Faster Breast Cancer Recurrence Risk Profiling: Supporting document accessed at: https://digistain.co.uk/ on 27 December 2023
5. Coombes, C., Angelou, C., Al-Khalili, Z. et al. Performance of a novel spectroscopy-based tool for adjuvant therapy decision-making in hormone receptor-positive breast cancer: a validation study. Breast Cancer Res Treat (2024). https://doi.org/10.1007/s10549-023-07229-y
6. Breast cancer diagnostic tool could save NHS £287m. Accessed from: https://www.med-technews.com/news/Digital-in-Healthcare-News/breast-cancer-diagnostic-tool-could-save-nhs-%C2%A3287m/ on 27 December 2023.

Prepared by

Dr. Ana Fizalinda Abdullah Sani
Senior Principal Assistant Director
Health Technology Assessment Section (MaHTAS)
Medical Development Division
Ministry of Health Malaysia

Reviewed by

Dr. Izzuna Mudla Mohamed Ghazali
Deputy Director & Public Health Physician
Malaysian Health Technology Assessment Section (MaHTAS)
Medical Development Division
Ministry of Health Malaysia

28 January 2024