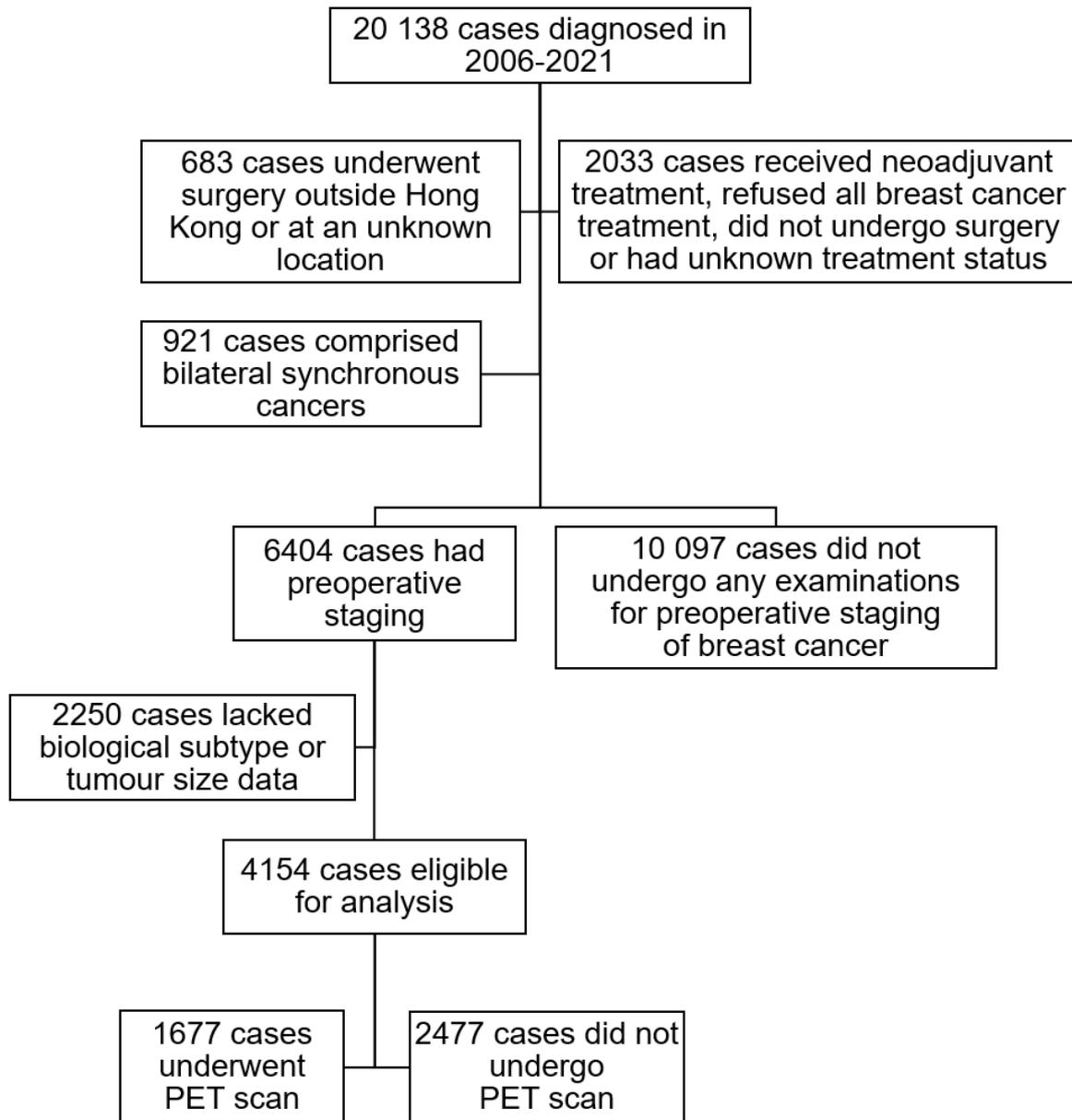


Supplementary material

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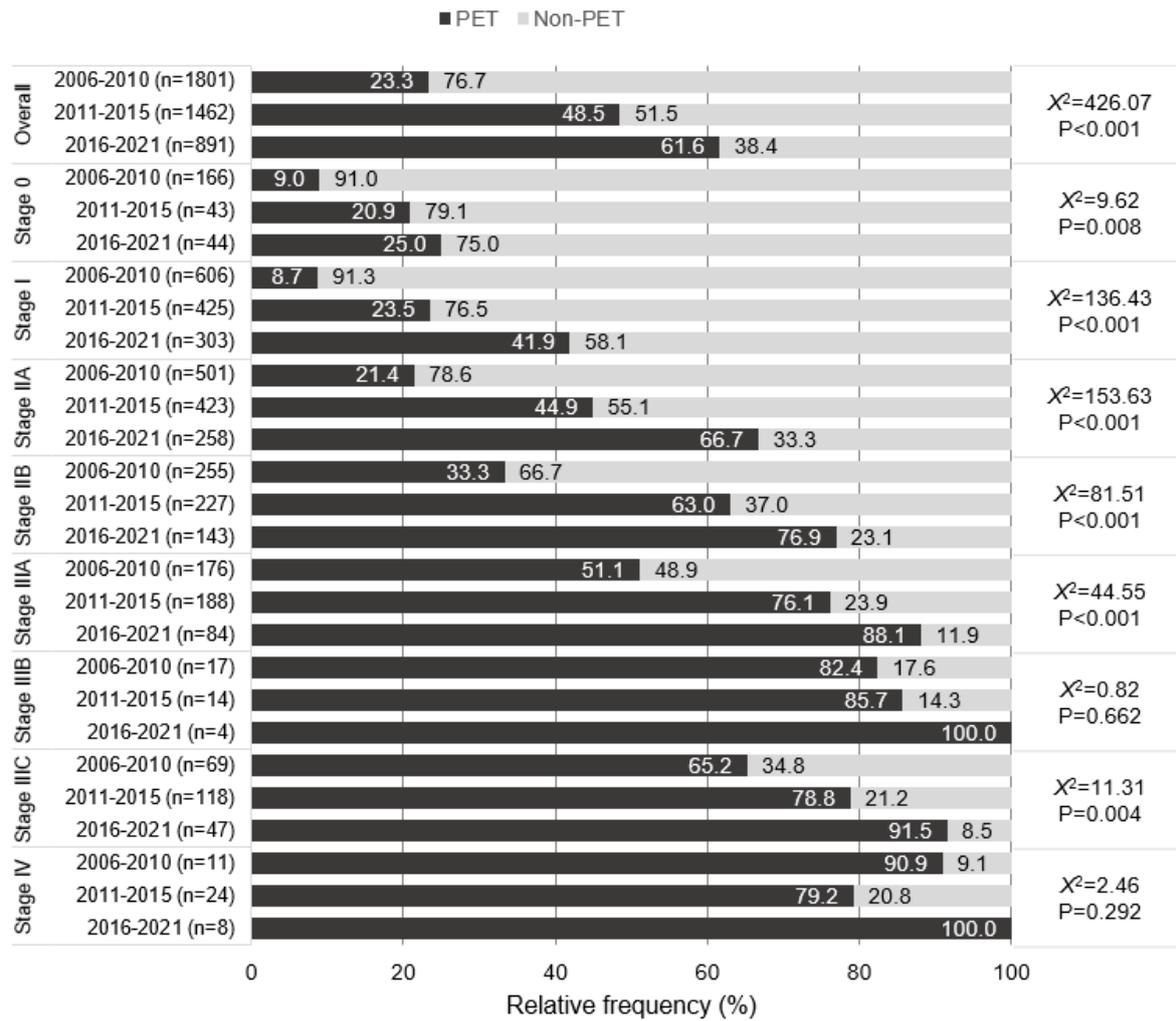
Supplement to: CCH Kwok, HCY Wong, CYH Wong, et al. Use of ¹⁸F-fluorodeoxyglucose positron emission tomography coupled with computed tomography in early breast cancer management: consensus-based local recommendations by the Hong Kong Breast Cancer Foundation PET/CT Study Group. Hong Kong Med J 2025;Epub 12 Nov 2025. <https://doi.org/10.12809/hkmj2411789>.

Supplementary Figure 1. Retrieval of eligible female patients diagnosed with breast cancer since 2006 from the Hong Kong Breast Cancer Registry database to analyse the utilisation of positron emission tomography scans over the period 2006-2021



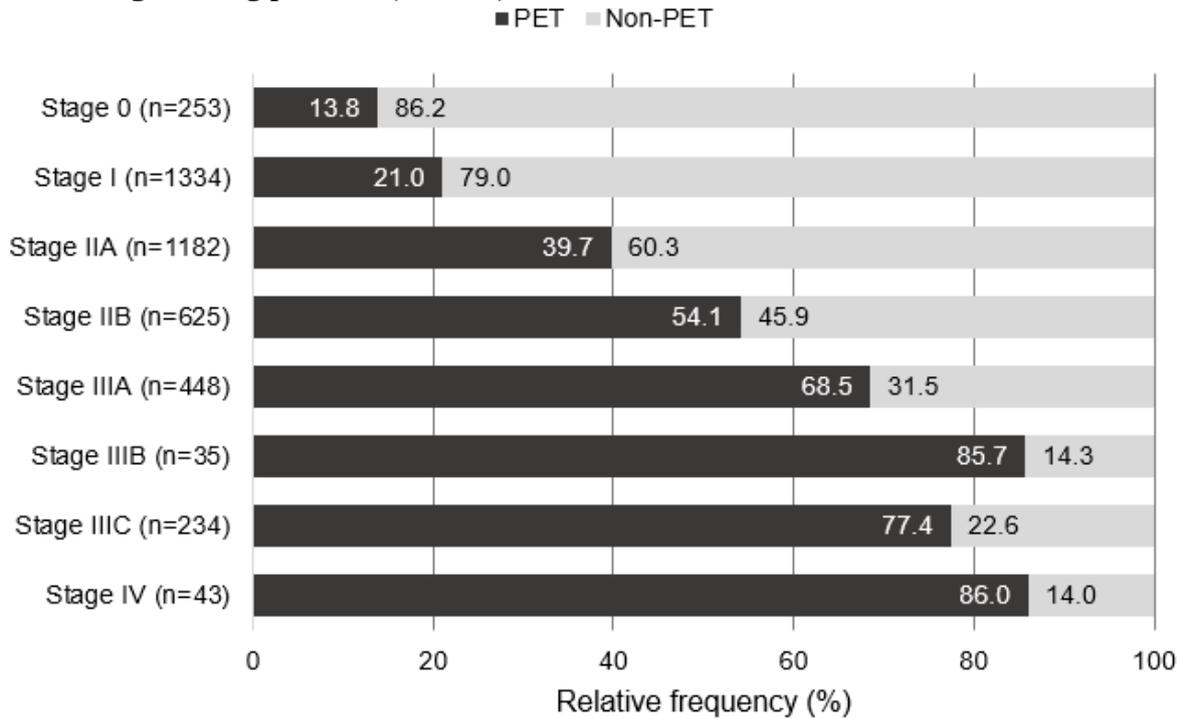
Abbreviation: PET = positron emission tomography

Supplementary Figure 2. Use of positron emission tomography scans by pathological cancer stage and trends across three cohorts (n=4154)



Abbreviation: PET = positron emission tomography

Supplementary Figure 3. Use of positron emission tomography scans by pathological cancer stage among patients (n=4154)*



Abbreviation: PET = positron emission tomography

* Most patients had early-stage breast cancer: 81.7% for stage 0 + I + IIA + IIB versus 18.3% for stage IIIA + IIIB + IIIC + IV. PET scans were more commonly performed for patients with stage III (including IIIA, IIIB, and IIIC) [72.2%] and stage IV (86.0%), followed by stage IIA and IIB (44.7%). However, PET scans were also performed for stage 0 (13.8%) and stage I cancers (21.0%)

Appendix 1. Evidence summary sheet presented to invited experts

Recommendation 1: ^{18}F -FDG-PET/CT scan is not recommended for breast cancer screening.

Supporting evidence: In a Korean retrospective study investigating which clinical variables differentiate between benign and malignant breast lesions,¹ across 91 lesions in 82 patients with incidental findings of breast uptake on PET/CT, only 29.7% of lesions were malignant. The only factor that allowed differentiation between benign and malignant lesions was the BI-RADS score using mammography and ultrasound. This finding suggests that conventional breast imaging is more helpful in distinguishing benign from malignant lesions.

Recommendation 2: ^{18}F -FDG-PET/CT scan is not recommended for staging patients with DCIS and clinical or pathological stage I breast cancer.

Supporting evidence: The risk of distant metastases in T1N0 disease (stage I of AJCC) is very low (similar to the risk for DCIS). In a study of 325 operable patients with mostly T1 disease, ^{18}F -FDG-PET scans (without a CT component) identified suspicious lesions in 13 patients.² Ultimately, only three (0.9%) were confirmed as metastatic disease; the remainder were false-positives.² In patients with stage I breast cancer, such workup could delay therapeutic management and/or cause unnecessary anxiety.

Recommendation 3: ^{18}F -FDG-PET/CT is not recommended to assess breast cancer multifocality.

Supporting evidence: Positron emission tomography coupled with CT has lower sensitivity for detecting multifocality compared with MRI. Ergul et al³ reported sensitivities of 67% for PET/CT and 78% for MRI.

Recommendation 4: ^{18}F -FDG-PET/CT is not recommended to guide axillary management in clinical N0 stage patients.

Supporting evidence: Sensitivity for axillary lymph node detection is low in patients with small tumours. A meta-analysis and systematic review of 25 studies investigating the accuracy of PET/CT compared with SLNB showed that PET/CT was inferior to SLNB.⁴

Revised Recommendation 4: ^{18}F -FDG-PET/CT is not recommended to guide axillary management in patients with no evidence of axillary involvement on clinical examination, ultrasound and/or MRI, and planned upfront surgery.

Recommendation 5: ^{18}F -FDG-PET/CT is recommended over multimodality investigations (eg, contrast CT, MRI, and bone scan) for preoperative staging in clinical stage IIB or above to detect extra-axillary regional lymph nodes and distant metastases.

Supporting evidence: In a multicentre randomised controlled trial, Dayes et al⁵ demonstrated that among patients with clinical stage IIB or above, a significantly larger proportion were upstaged to stage IV with PET/CT relative to conventional imaging (ie, bone scan and CT of the thorax, abdomen, and pelvis).

Recommendation 6: ^{18}F -FDG-PET/CT can be considered in selected patients with clinical stage IIA (T1N1 or T2N0) disease with high-risk histological features (eg, ER- or PR-negative, HER2-positive, and high Ki-67 level) to detect extra-axillary regional lymph nodes and distant metastases.

Supporting evidence: A systematic review and meta-analysis showed that primary tumour SUV_{max} is significantly higher in ER-negative, PR-negative, HER2-positive, and Ki-67–positive breast cancer patients.⁶ Positron emission tomography coupled with CT may detect occult metastases that are not identified by other imaging modalities, such as chest X-ray and contrast-enhanced computed tomography. This recommendation aligns with the 2023 NCCN breast cancer guideline.⁷

Recommendation 7: ^{18}F -FDG-PET/CT is not recommended to assess local tumour response to neoadjuvant systemic treatment in the breast to guide surgical planning.

Supporting evidence: In a systematic review and meta-analysis published in 2018,⁸ MRI displayed higher diagnostic accuracy than PET/CT in predicting pathological response among breast cancer patients undergoing neoadjuvant systemic treatment. In patients with planned tumour downstaging to allow breast-conserving therapy, PET/CT may not be the optimal modality for response assessment.

Revised Recommendation 7: ^{18}F -FDG-PET/CT is not recommended to assess whether the extent of tumour shrinkage in the breast after neoadjuvant systemic treatment is adequate to consider breast-conserving therapy.

Recommendation 8: ^{18}F -FDG-PET/CT is not recommended to guide the decision for axillary lymph node dissection in patients with clinically node-positive disease who become clinically node-negative after neoadjuvant systemic therapy.

Supporting evidence: In a systematic review and meta-analysis published in 2021,⁹ the pooled sensitivity, specificity, positive predictive value, and negative predictive value of ¹⁸F-FDG-PET/CT for predicting pathological complete response in patients were 38%, 86%, 78%, and 49%, respectively. The high false-positive and false-negative rates make ¹⁸F-FDG-PET/CT unreliable for determining whether patients can directly omit or proceed with axillary lymph node dissection. Additional investigations, such as SLNB, may be required to guide decisions on axillary lymph node dissection.

Revised Recommendation 8: ¹⁸F-FDG-PET/CT is not recommended to guide the decision for axillary lymph node dissection in patients with clinically node-positive disease who become node-negative on clinical examination and ultrasound and/or MRI after neoadjuvant systemic therapy.

Recommendation 9: ¹⁸F-FDG-PET/CT is recommended to screen for breast cancer recurrence in patients with suspicious symptoms or signs and/or elevated tumour markers.

Supporting evidence: A systematic review and meta-analysis summarised the overall diagnostic value of ¹⁸F-FDG-PET or PET/CT for detecting recurrence in breast cancer patients with symptoms or signs suggestive of recurrence.¹⁰ The pooled sensitivity was 0.90 (95% CI=0.88-0.92), and the pooled specificity was 0.81 (95% CI=0.78-0.84).¹⁰ In a retrospective study of 77 asymptomatic breast cancer patients with elevated CA15-3 level, the sensitivity, specificity, positive predictive value, and negative predictive value of PET/CT for detecting recurrence were 98%, 88%, 96%, and 94%, respectively.¹¹ Relative to conventional imaging techniques, Dong et al¹² reported that the diagnostic accuracy of PET/CT was significantly higher in patients with elevated tumour markers.

Recommendation 10: Routine surveillance for breast cancer recurrence with ¹⁸F-FDG-PET/CT is not recommended.

Supporting evidence: In a large retrospective study of 1681 asymptomatic breast cancer patients who had completed surgery and adjuvant treatments, then were offered PET/CT surveillance, the detection rate of positive results was 5%, with nearly a 30% likelihood of false-positive findings.¹³

Abbreviations: ¹⁸F-FDG-PET/CT = ¹⁸F-fluorodeoxyglucose positron emission tomography coupled with computed tomography; 95% CI = 95% confidence interval; AJCC = American Joint Committee on Cancer; BI-RADS = Breast Imaging Reporting and Data System; CT = computed tomography; DCIS = ductal

carcinoma in situ; ER = oestrogen receptor; HER2 = human epidermal growth factor receptor 2; MRI = magnetic resonance imaging; NCCN = National Comprehensive Cancer Network; PR = progesterone receptor; SLNB = sentinel lymph node biopsy; SUV_{max} = maximum standardised uptake value

References

1. Shin KM, Kim HJ, Jung SJ, et al. Incidental breast lesions identified by ^{18}F -FDG PET/CT: which clinical variables differentiate between benign and malignant breast lesions? *J Breast Cancer* 2015;18:73-9.
2. Pritchard KI, Julian JA, Holloway CM, et al. Prospective study of 2- $[^{18}F]$ fluorodeoxyglucose positron emission tomography in the assessment of regional nodal spread of disease in patients with breast cancer: an Ontario clinical oncology group study. *J Clin Oncol* 2012;30:1274-9.
3. Ergul N, Kadioglu H, Yildiz S, et al. Assessment of multifocality and axillary nodal involvement in early-stage breast cancer patients using ^{18}F -FDG PET/CT compared to contrast-enhanced and diffusion-weighted magnetic resonance imaging and sentinel node biopsy. *Acta Radiol* 2015;56:917-23.
4. Peare R, Staff RT, Heys SD. The use of FDG-PET in assessing axillary lymph node status in breast cancer: a systematic review and meta-analysis of the literature. *Breast Cancer Res Treat* 2010;123:281-90.
5. Dayes IS, Metser U, Hodgson N, et al. Impact of ^{18}F -labeled fluorodeoxyglucose positron emission tomography-computed tomography versus conventional staging in patients with locally advanced breast cancer. *J Clin Oncol* 2023;41:3909-16.
6. de Mooij CM, Ploumen RA, Nelemans PJ, Mottaghy FM, Smidt ML, van Nijnatten TJ. The influence of receptor expression and clinical subtypes on baseline $[^{18}F]$ FDG uptake in breast cancer: systematic review and meta-analysis. *EJNMMI Res* 2023;13:5.
7. Gradishar WJ, Moran MS, Abraham J, et al. NCCN Guidelines[®] Breast Cancer Version 4.2023. *J Natl Compr Canc Netw* 2023;21:594-608.
8. Li H, Yao L, Jin P, et al. MRI and PET/CT for evaluation of the pathological response to neoadjuvant chemotherapy in breast cancer: a systematic review and meta-analysis. *Breast* 2018;40:106-15.
9. Samiei S, de Mooij CM, Lobbes MB, Keymeulen KB, van Nijnatten TJ, Smidt ML. Diagnostic performance of noninvasive imaging for assessment of axillary response after neoadjuvant systemic therapy in clinically node-positive breast cancer: a systematic review and meta-analysis. *Ann Surg* 2021;273:694-700.
10. Xiao Y, Wang L, Jiang X, She W, He L, Hu G. Diagnostic efficacy of ^{18}F -FDG-PET or PET/CT in breast cancer with suspected recurrence: a systematic review and meta-analysis. *Nucl Med Commun* 2016;37:1180-8.
11. Göktaş İ, Cayvarlı H. The role of ^{18}F -FDG PET/CT in evaluating elevated levels of tumor

markers in breast cancer. *Mol Imaging Radionucl Ther* 2018;27:3-9.

12. Dong Q, Wu X, Gan W, et al. Construction and validation of web-based nomograms for detecting and prognosticating in prostate adenocarcinoma with bone metastasis. *Sci Rep* 2022;12:18623.
13. Lee H, Choi JY, Park YH, et al. Diagnostic value of FDG PET/CT in surveillance after curative resection of breast cancer. *Cancers (Basel)* 2023;15:2646.

Appendix 2. Expert panel members

First name	Last name	Specialty
Ying Wing Jessie	Chan	Surgeon
Yolanda	Chan	Surgeon
Chun Hin	Chan	Oncologist
Wendy	Chan	Oncologist
Miranda	Chan	Surgeon
Man Yi	Chan	Surgeon
Sau Ying Jenny	Chan	Surgeon
Amy	Chang	Oncologist
Pui Ling	Chau	Surgeon
Thomas	Cheng	Nuclear medicine radiologist
Foon Yiu	Cheung	Oncologist
Kwok Fai	Cheung	Surgeon
Polly	Cheung	Surgeon
Ying Wah	Chiu	Surgeon
Joanne	Chiu	Oncologist
Lai Yin Catherine	Choi	Surgeon
Chi Yee	Choi	Surgeon
Sara	Fung	Surgeon
Chiu Ming	Ho	Surgeon
Yan Ho	Hui	Nuclear medicine radiologist
Wai Ka	Hung	Surgeon
Ka Wai Ray	Hung	Surgeon
Iris Ka Ming	Wong	Oncologist
Boom Ting	Kung	Nuclear medicine radiologist
Wing Yu Jessica	Lai	Oncologist
Yeung Kit Billy	Lam	Surgeon
Stephanie	Lau	Surgeon
Tsz Shan	Lau	Oncologist
Thomas	Lau	Oncologist
Siu King	Law	Surgeon
Ka Suet	Law	Oncologist
Chun Key	Law	Oncologist
Lawrence Pui Ki	Li	Oncologist
Ho Yin Henry	Lee	Surgeon
Andrea	Lee	Surgeon

Kwong Chuen	Leung	Oncologist
Sheona	Leung	Oncologist
Kwok Cheung Alex	Leung	Oncologist
Kwan Ho	Leung	Oncologist
Roland	Leung	Oncologist
Eric	Leung	Nuclear medicine radiologist
Yeuk Hei Ida	Ling	Surgeon
Kwok Kuen	Ma	Surgeon
Lorraine Wai Yan	Ma	Surgeon
Chun Hin Tommy	Man	Surgeon
Ting Ying	Ng	Oncologist
Roger	Ngan	Oncologist
Mimi	Poon	Surgeon
Robin	Sheung	Surgeon
Tracy	Shum	Oncologist
Lai Shan Diana	Siu	Oncologist
Sung Inda	Soong	Oncologist
Dacita	Suen	Surgeon
Susanna	Tam	Surgeon
Cheuk Ho Gordon	Tang	Oncologist
Winnie	Tin	Oncologist
Yee Yan Yvonne	Tsang	Surgeon
Janice	Tsang	Oncologist
Violet	Tsoi	Surgeon
Cindy	Wong	Oncologist
Ting	Wong	Radiologist
Hedwig	Wong	Surgeon
Tak Man	Wong	Surgeon
Lai Shan	Wong	Surgeon
Catherine Yuet Hung	Wong	Nuclear medicine radiologist
Ting Ting	Wong	Surgeon
Chun Chung	Yau	Oncologist
Tsz Kok	Yau	Oncologist
Winnie	Yeo	Oncologist
Nga Yan	Yeung	Oncologist
Ho Yan	Yuen	Surgeon