IAEA-CN410-IPET 20424

IAEA

INTERNATIONAL CONFERENCE ON HYBRID IMAGING

IPET 2024

NOVELTY OF 18F–FLUOROCHOLINE COMPUTED-TOMOGRAPHY (18-FCHPETCT) IN PREDICITING QUALITY OF LIFE IN MALIGNANT BREAST CANCER PATIENTS.

MOHD HAZEMAN ZAKARIA – PRESENTER

FATHINUL FIKRI AHMAD SAAD

SHAHRUN NIZA ABDULLAH SUHAIMI

FACULTY OF MEDICINE & HEALTH SCIENCES, UNIVERSITI PUTRA MALAYSIA, MALAYSIA

FACULTY OF MEDICINE , UNIVERSITI KEBANGSAAN MALAYSIA, MALAYSIA

INTRODUCTION

- Breast cancer cases are increasing throughout the year.
- There are many radiotracers that available that used in PET / CT to ascertain the tumour landscapes of breast cancer.
- The use of FDG PET-CT marker becoming commonly used molecular imaging technique leads to poor diagnostic issues. The use of ^{18}F-FDG PET-CT is insensitive to detect malignant breast cancer types such as lobular carcinoma and detect the small volume lesion which low uptake of ^{18}F-FDG on PET/CT image.
- There were few studies which have looked into the role of 18FCH and breast cancer.
- The study of expression of choline tracer strategy is for staging and therapeutic response in breast cancer will give potential role in oncological imaging.

Literature Review

Signalling process that change the cellular landscape..

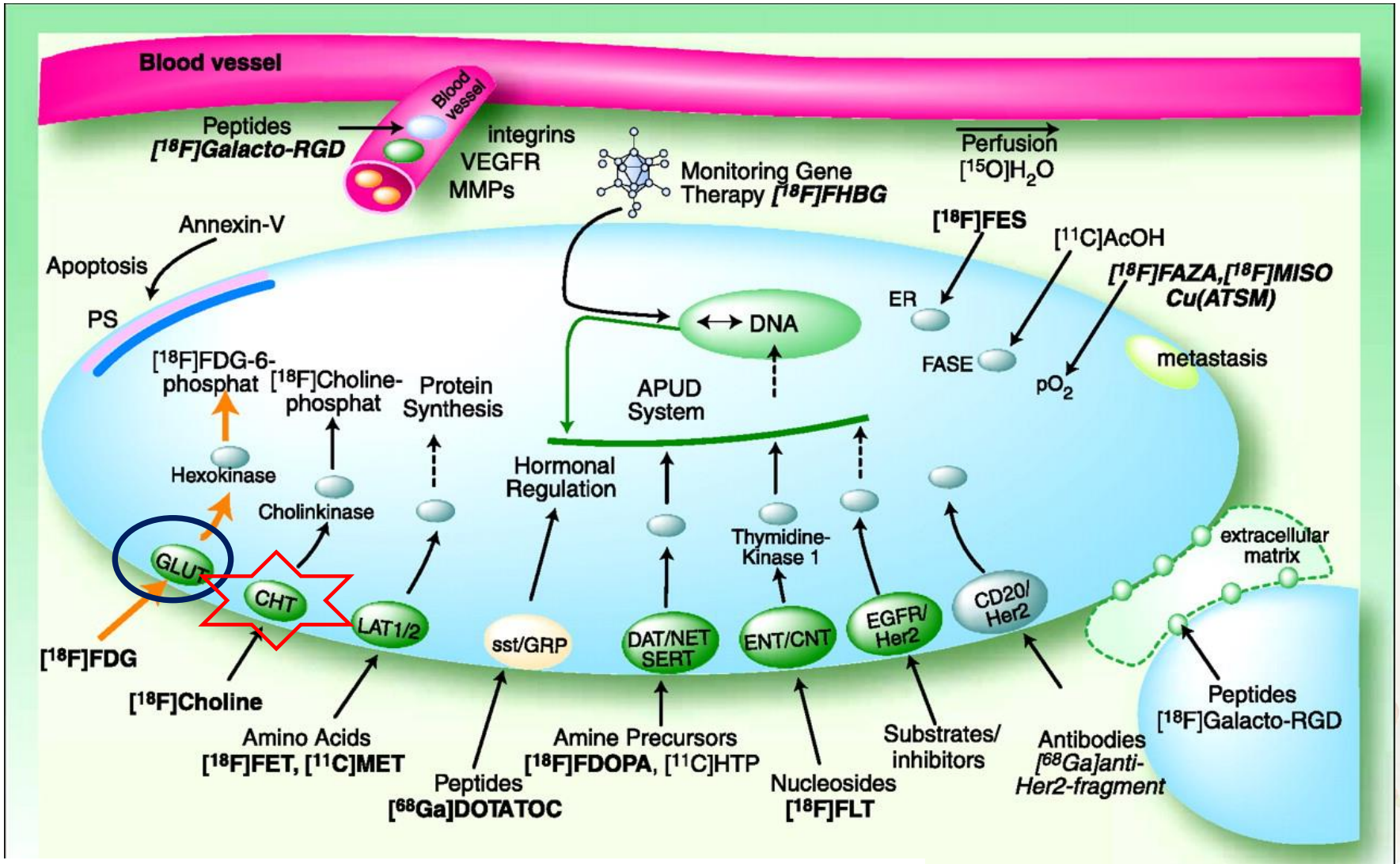


Figure 1 : Various pathways metabolism for radiotracers

IAEA International Atomic En

WHY WE USE 18-FCHOLINE ???

- Small volume sampling of FDG-negative malignancy.
- Lack of glutathione gene transporter in Global cell carcinoma (breast).
- Better noise-background ratio compared to FDG.

Tumour	FCH role	SUVmax	Published study
Breast cancer	Predictor for tumour aggressiveness	1.07-1.97	Damita et al. (2011)
Hepatocellular carcinoma	Predictor for recurrent tumour	0.94-2.1	Kwee S et al. (2007)
Prostate cancer	Predictor for malignancy	1.7-6.2	Tindall D et al. (2014)

Table 1 :FCH SUV max uptake variation in different cancers types which relatively low

POTENTIAL NEW TRACER 18 F-Flurocholine PET-CT

(ER+ve / PR-ve) or (ER-ve / PR+ve) + HER2 –ve → More aggressive tumour.

Bae et al. BMC Cancer (2015) 15:138
DOI 10.1186/s12885-015-1121-4

BMC Cancer

triple-negative breast cancer

Soo Youn Bae, Sangmin Kim, Jun Ho Lee, Hyun-chul Lee, Se Kyung Lee, Won Ho Kil, Seok Won Kim, Jeong Eon Lee and Seok Jin Nam*

The Journal of Nuclear Medicine is
SNMMI | Society of Nuclear Medicine and Molecular Imaging
1850 Samuel Morse Drive, Reston, VA 20190.
(Print ISSN: 0161-5505, Online ISSN: 2159-662X)

SNMMI SOCIETY NUCLEA AND M

Synthesis and Evaluation of ^{18}F-Labeled Choline Analogs as Oncologic PET Tracers

Timothy R. DeGrado, Steven W. Baldwin, Shuyan Wang, Matthew D. Orr, Ray P. Liao, Henry S. Friedman, Robert Reiman, David T. Price, and R. Edward Coleman

The preliminary imaging studies show excellent imaging feasibility of FCH in brain tumor, prostate cancer, and breast cancer. Clearly, further clinical studies on a larger

(Supplement 1):249

ical Diagnosis: Breast Cancer

Breast Cancer I: Horizons in Breast Cancer Imaging

Pilot study of 18F-fluorocholine uptake in normal and malignant breast tissue

Damita Thomas[1], Marc Coel[1], John Lim[1] and Sandi Kwee[1]

[1] Hamamatsu/Queen's PET Imaging Center, The Queen's Medical Center, Honolulu, HI

Conclusions: Although biopsy-confirmed breast cancers demonstrated a significant range of FCH uptake, detection was feasible due to relatively to low uptake in the surrounding breast tissue of both pre-and post- menopausal patients. To adequately evaluate relationships between FCH uptake and prognostic markers, further investigation using a larger patient sample is needed

New and novel radiotracer in PET / CT for breast cancer

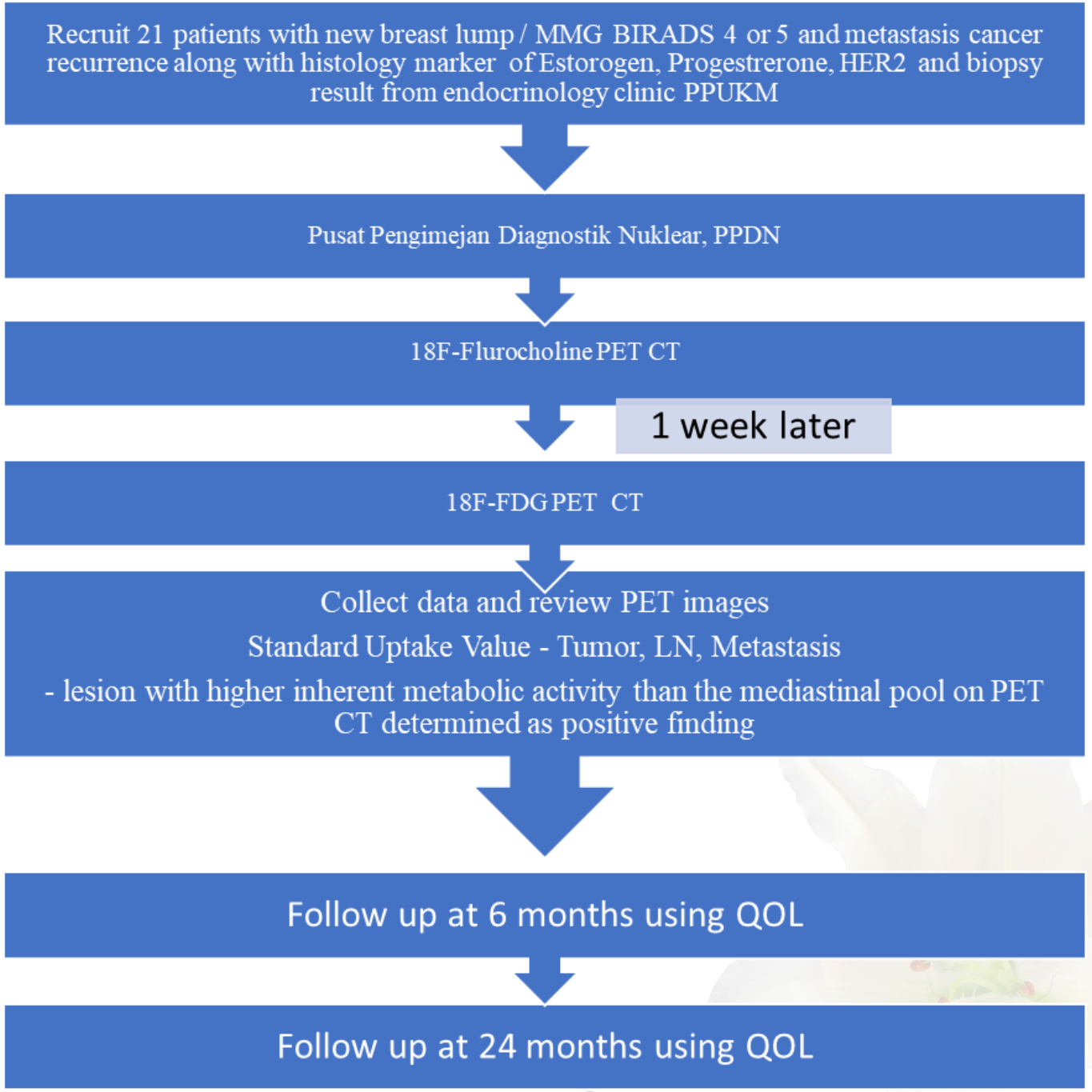
Tracer	Target mechanism	Applications	References
18F-fluorothymidine	Thymidine analog	Tumor proliferation imaging	(101, 102)
18F-FMISO	Hypoxic cells	Tumor hypoxia imaging	(6)
68Ga-NOTA-RM26	Targeting GRPR	ER+ tumor detection of proliferation phase patient	(103)
68Ga-BBN-RGD	Targeting GRPR and integrin αvβ3	Primary tumor and metastases detection, especially ER+ tumor	(104)
68Ga-NOTA-RGD	Targeting integrin αvβ3	Angiogenesis imaging, recurrence prediction and prognosis prediction	(105)
18F-Fluciclovine	Leucine analog	Primary tumor and metastases detection, NAC response prediction	(106–109)
68Ga-PSMA	Targeting tumor-specific antigen	TNBC and ASRC detection	(110–112)
18F-Fluorocholine	Cell membrane component	Primary tumor and metastases detection	(113, 114)
68Ga-NO2AP-BP	Macrocyclic chelator	Skeletal metastases detection	(115)
89Zr-trastuzumab	Targeting HER2	HER2+ tumor detection	(116)
64Cu-DOTA-trastuzumab	Targeting HER2	HER2+ primary tumor and metastases detection	(117, 118)
89Zr-Pertuzumab	Targeting HER2	HER2+ primary tumor and metastases detection	(119)
68Ga-ABY-025	Targeting HER2	HER2+ tumor detection	(120)
18F-FES	Targeting ER	ER+ tumor, endocrine therapy monitoring and prognosis prediction	(121–123)
68Ga-DOTATATE	Targeting somatostatin receptor	Exclusion of fibroadenoma	(124)

TNBC, triple-negative breast cancer; ASRC, signet ring cell breast adenocarcinoma; GRPR, gastrin-releasing peptide receptor; FES, 16α-17β-fluoroestradiol; FMISO, fluoromisonidazole; NO2AP-BP, triazacyclononane bisphosphonate.

Table 2 : New and novel radiotracer in PET / CT for breast cancer
Source: Progress and Future Trends in PET/CT and PET/MRI Molecular Imaging Approaches for Breast Cancer by Yue Miming et al in 2020.

IAEA
International Atomic Energy Agency

METHODOLOGY



IAEA
International Atomic Energy Agency

Quality Of Life Data

- The patients will follow up at 6 months and 24 months.
- It later incorporated into for QOL domains – Global Health Status (GHS), Physical function (PF), Role Function (RF) and Social function (SF) according to the EORTC quality of life questionnaire (QLQ) which is is an integrated system for assessing the healthrelated quality of life (QoL) of cancer.

Reference : based on European Organisation for Research and Treatment of Cancer (EORTC)

* *Use of the SF-36®, SF36v2®, SF-12® and SF-12v2® Questionaires which are trademarks of Medical Outcome Trust and are used under license. The SF-25v2®Heal is copyrighted by Quality Metric Incorporated. The patient was facilitated to answer the questionaires through interview.*

Scoring system :

- The patients are categorised into satisfactory and unsatisfactory based by marks by the questionnaires. The score is from 1 to 5 indicating from bad to good score. Overall, the patient will determine where they have satisfactory which score 0 and satisfactory which score 1.

RESULTS

- There is a high sensitivity and specificity of 18-FCHPET/CT in both breast lesions with 40% and 68.8% compared to 18-FDGPET/CT with 33.3% and 66.7%.
- Besides that, lymph nodes and metastasis distant 18-FDGPET/CT showed high sensitivity and specificity compared to 18-FCHPET/CT.

Imaging	Primary tumour		PPV	NPV	Lymph node		PPV	NPV	Metastasis		PPV	NPV
	Sensitivity	Specificity			Sensitivity	Specificity			Sensitivity	Specificity		
FDG	33.3%	66.7%	33.3	50.3	66.7%	83.3%	40	50	42.9%	92.9%	23.1	50
FCH	40%	68.8%	36.8	50.0	44.5%	70%	31.8	50	27.3%	90%	15.2	50

PPV : Positive Predictive Value
NPV : Negative Predictive Value

Table 3 : The Sensitivity and Specificity of 18-FCH/PETCT Compared to 18F-FDG in Both Breast Lesions, Lymph Node and Metastasis Distant

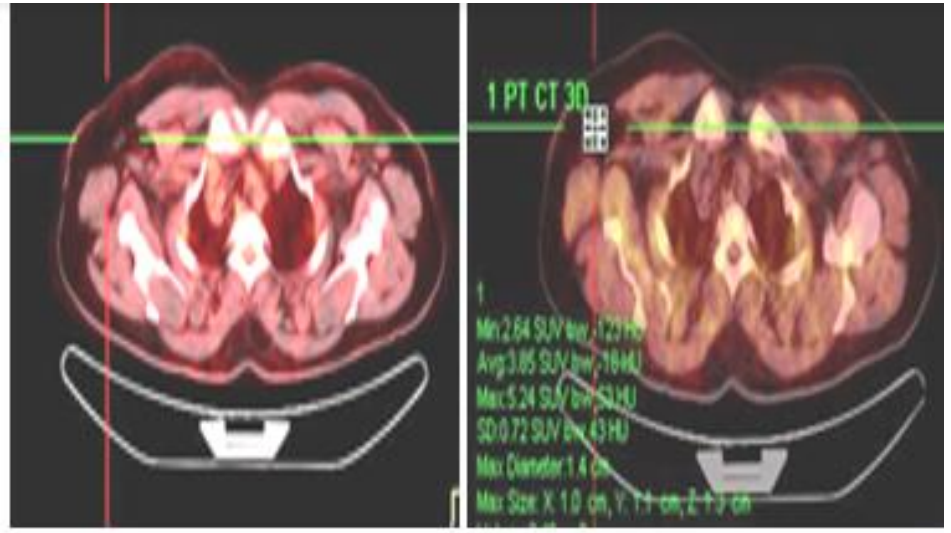
IAEA International Atomic Energy Agency

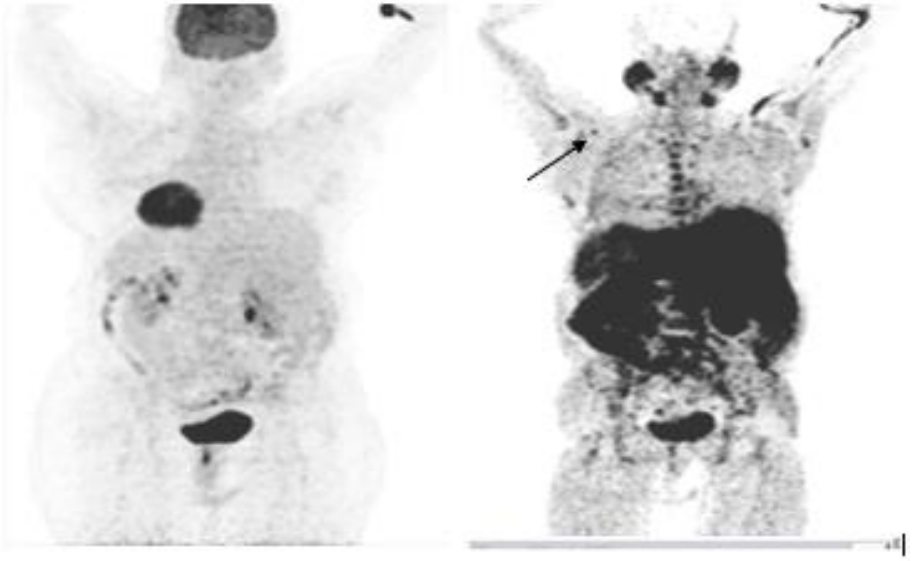
PET/CT mean±SD	Local right breast	p	Local left breast	p	Lymph node	p	Metastasis	p
FDG	1.92±0.97	0.15	1.78±0.99	0.26	1.53±1.7	0.32	1.74±2.32	0.004
FCH	1.34±1.01		0.97±0.81		1.28±1.90		2.27±3.19	

- There is significant different in distant metastasis on mean of 18F-FCH - 2.27±3.19 Vs 18F-FDG 1.74±2.32, p=0.004.

FDG

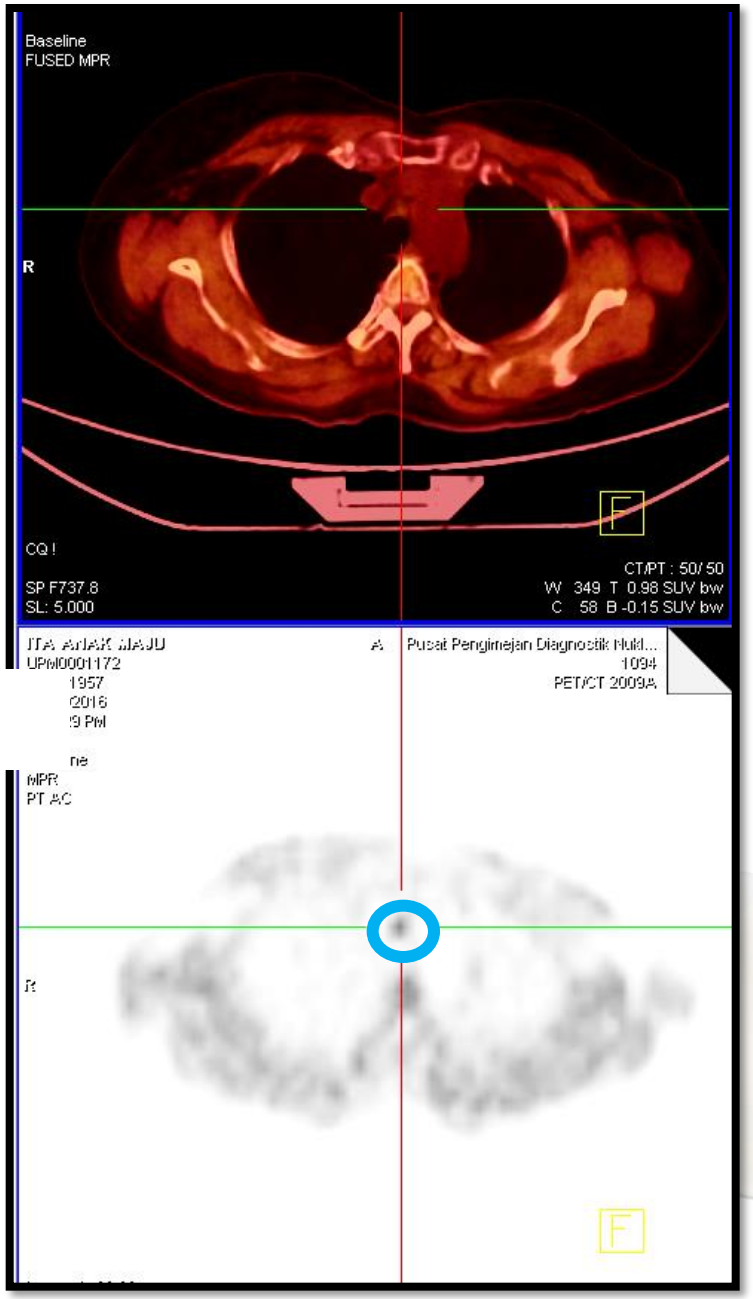
FCH



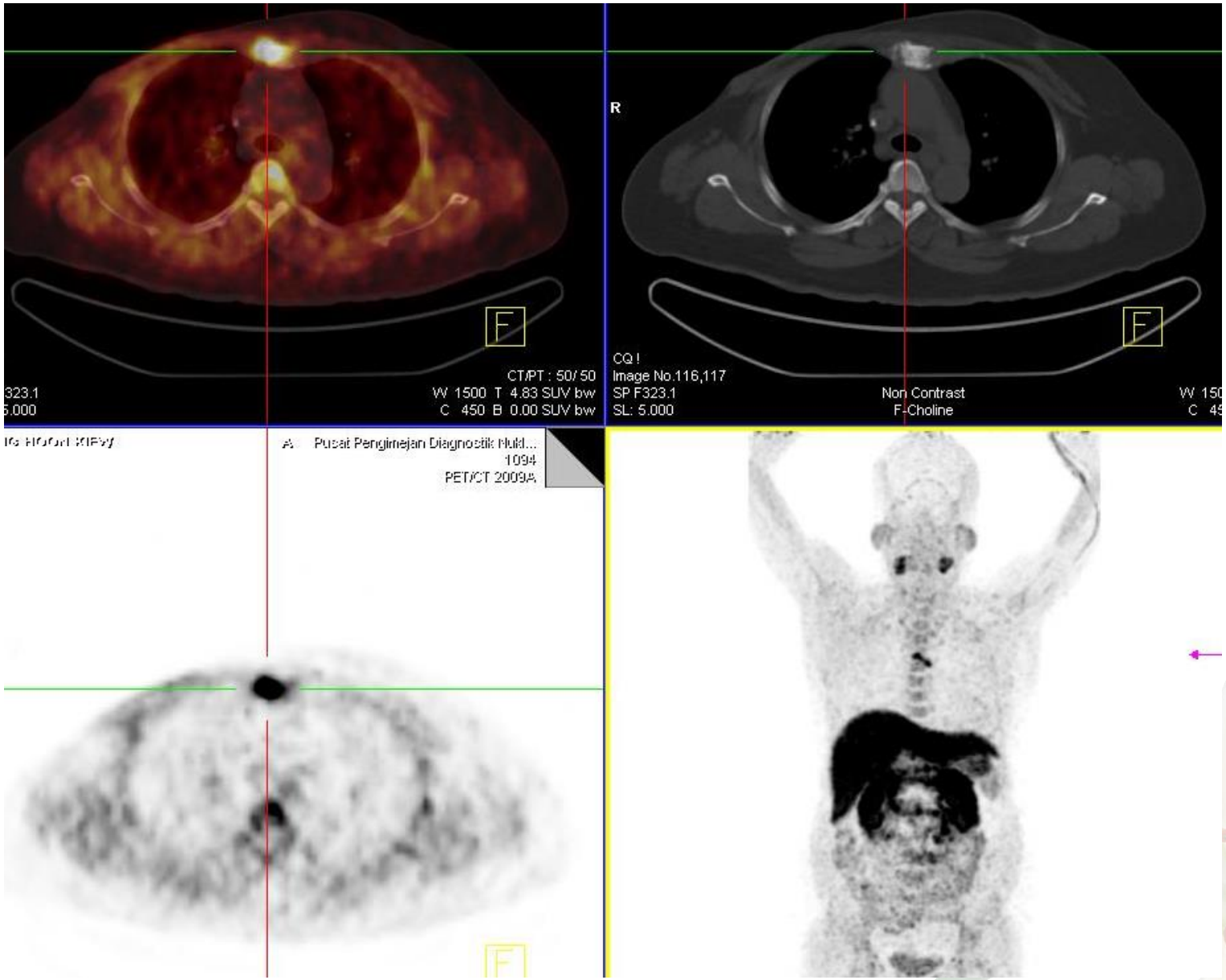


Images above showing Positive FCH (right) with SUVmax:5.24 in lymph node metastasis and negative FDG (left) in patients with diagnosis of invasive ductal carcinoma

- Positive Node in 18-FCH in breast cancer.



Bone Metastasis



RESULT

N	Age	BMI	Birads	Biopsy	Histology		
					ER	PR	HER2
1	56	27.69	4.00	IDC	+	+	+
2	59	24.06	4.00	IDC	+	+	-
3	55	25.11	4.00	benign	-	-	+
4	73	24.84	4.00	IDC	+	+	-
5	46	23.91	4.00	IDC	+	+	-
6	60	23.38	4.00	IDC	+	+	+
7	48	20.25	4.00	benign	-	-	-
8	47	25.68	4.00	IDC	+	+	+
9	48	33.95	4.00	IDC	+	+	+
10	62	32.37	5.00	IDC	+	+	-
11	53	20.08	4.00	IDC	+	+	-
12	64	30.36	4.00	IDC	+	+	-
13	69	28.62	4.00	benign	-	-	-
14	40	20.28	4.00	IDC	+	+	+
15	36	29.62	4.00	IDC	+	+	-
16	41	28.23	4.00	IDC	+	+	+
17	41	31.24	4.00	IDC	+	+	-
18	57	37.78	4.00	IDC	-	-	+
19	80	30.73	4.00	IDC	-	-	+
20	69	20.43	4.00	IDC	-	-	+
21	40	23.51	4.00	IDC	-	-	-

There was a significant different between 18-FCH SUVmax of the HER2-ve and the HER2+ve (1.99±1.52g/dl vs 0.2±0.22g/dl; $p<0.05$).

Bae et al. BMC Cancer (2015) 15:138
DOI 10.1186/s12885-015-1121-4

BMC Cancer

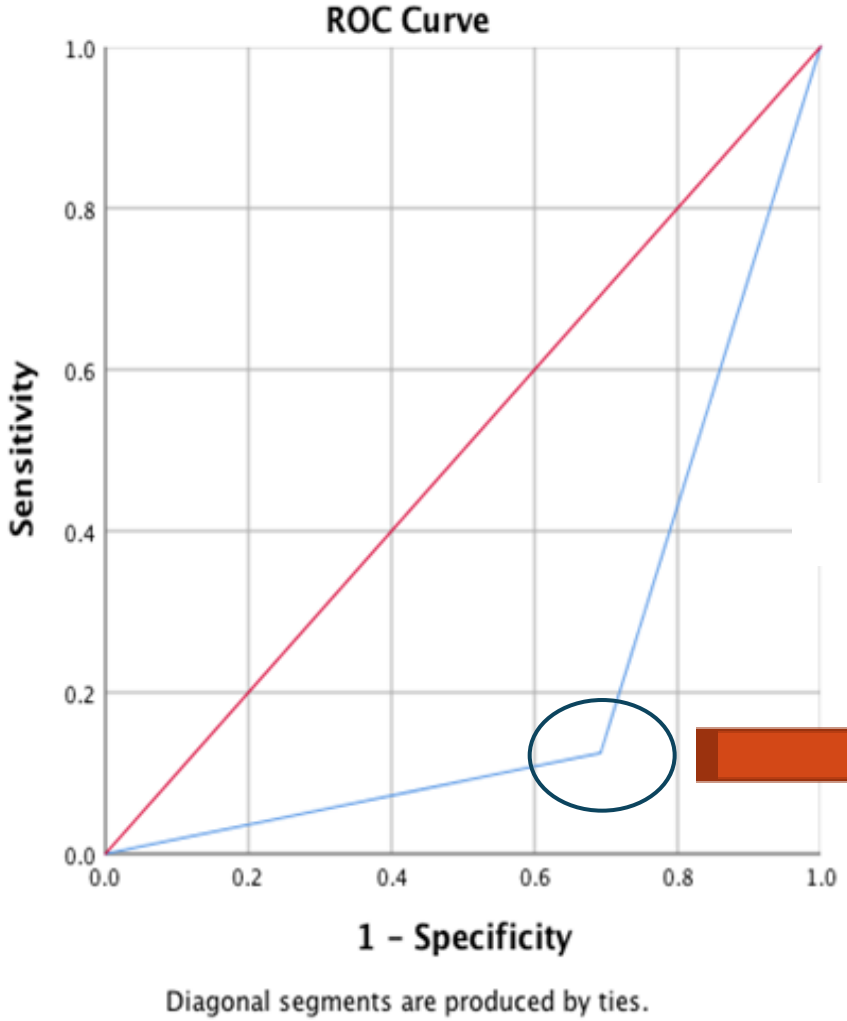
RESEARCH ARTICLE Open Access

Poor prognosis of single hormone receptor-positive breast cancer: similar outcome as triple-negative breast cancer

Soo Youn Bae, Sangmin Kim, Jun Ho Lee, Hyun-chul Lee, Se Kyung Lee, Won Ho Kil, Seok Won Kim, Jeong Eon Lee and Seok Jin Nam*

IAEA International Aton

(ER+ve / PR-ve) or (ER-ve / PR+ve) + HER2 –ve → More aggressive tumour.



Symmetric Measures (N = 21)			
	Method	SUV value	Approximate Significance
Nominal by Nominal	Contingency Coefficient	0.599	0.001
Interval by Interval	Pearson's R	0.748	.000
Ordinal by Ordinal	Spearman Correlation	0.748	.000
Measure of Agreement	Kappa	0.734	0.001

Significant when $p < 0.05$

0.75

The cut off value for 18-FCHPET/CT in determining the breast cancer aggressiveness when the SUV more than 0.75

IAEA
International Atomic Energy Agency

RESULT

- High SUVmax 18-FCH PET/CT for the malignant histological subtype is at the cut-off value of 0.75 ($p<0.05$, specificity = 0.43) which indicate the more aggressive the tumour.
- The value of SUVmax 18-FCH PET/CT > 0.75 ➡ MORE AGGRESSIVE TUMOUR

Tumour	FCH role	SUVmax	Published study
Breast cancer	Predictor for tumour aggressiveness	1.07-1.97	Damita et al. (2011)
Hepatocellular carcinoma	Predictor for recurrent tumour	0.94-2.1	Kwee S et al. (2007)
Prostate cancer	Predictor for malignancy	1.7-6.2	Tindall D et al. (2014)

RESULT

To determine the association of 18-FCHPET with Quality of Life (QOL) in patient with aggressive breast cancer phenotype.

A 6 months

QOL Scores	GHS	PF	RF	SF
FCH (High Vs Low)	1.667	8.067	3.267	5.4
Asymp. Sig.	0.197	0.005	0.71	0.02

Significant when p<0.05
GHS : Global Health Status ,
PF : Physical Function,
RF : Role Function
SF : Social Function
The score 1- 5 : Poor – Good)
Based on questionnaires in Appendix C

We follow up patients 6 months, there is association significant association of categorized predict SUV (>0.75) with QOL domains (physical and social domains).

IAEA
International Atomic Energy Agency

RESULT

A 24 months

QOL Scores	GHS	PF	RF	SF
FCH (High Vs Low)	0.67	1.00	0.67	1.00
Asymp. Sig.	0.796	1.00	0.796	1.00

Significant when p<0.05
GHS: Global Health Status
PF: Physical Function,
RF: Role Function
SF: Social Function
The score 1- 5: Poor – Good)
Based on questionnaires in Appendix C

In contrast, there no association significant of categorized predict SUV ((>0.75) with QOL scores domains at 24 months.

We conclude that the predict cut off SUV of > 0.75 is very potent predictive marker for determine breast cancer aggressiveness. This surrogate marker is very potent in determine the association with the QOL domains particularly at 6 months.

CONCLUSION

- Utility of 18-FCH PET/CT is a potential predictive marker (dual tracer-complementary to FDG) in determining breast cancer aggressiveness in view of the lipid metabolism signalling pathway (better N:B ratio, high specificity metastasis in our cohort and non-Glut-1 cancer landscape)
- The value of SUVmax 18-FCH PET/CT is associated with more aggressive breast cancer when the value predictive 0.75.
  - Use to determine the QOL of breast cancer patient in 6 months time post imaging.
- Hence, the 18-FCH PET/CT is potential surrogate marker to determine the breast cancer aggressiveness and QOL of breast cancer patients.

UNIVERSITI PUTRA MALAYSIA
BERILMU BERBAKTI

TERIMA KASIH/*THANK YOU*

www.upm.edu.my

BERILMU BERBAKTI
WITH KNOWLEDGE WE SERVE

IAEA
International Atomic Energy Agency

IAEA

INTERNATIONAL CONFERENCE
ON HYBRID IMAGING

IPET 2024

Thank you!