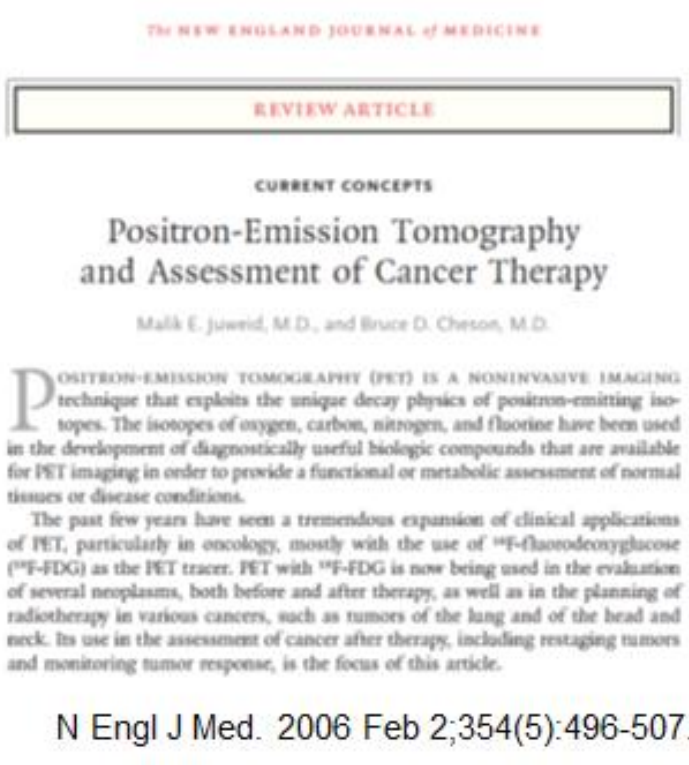
タイトル

18F-fluorodeoxyglucose Positron Emission Tomography Optimizes Neoadjuvant Chemotherapy for Primary Breast Cancer to Achieve Pathological Complete Response.

18F-フルオロデオキシグルコース ポジトロン エミッショントモグラフィ（FDG PET）の使用により、原発性乳がんが病理学的完全奏効になるための術前化学療法を最適化することが可能となる。

大学院生　上田重人


The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

CURRENT CONCEPTS

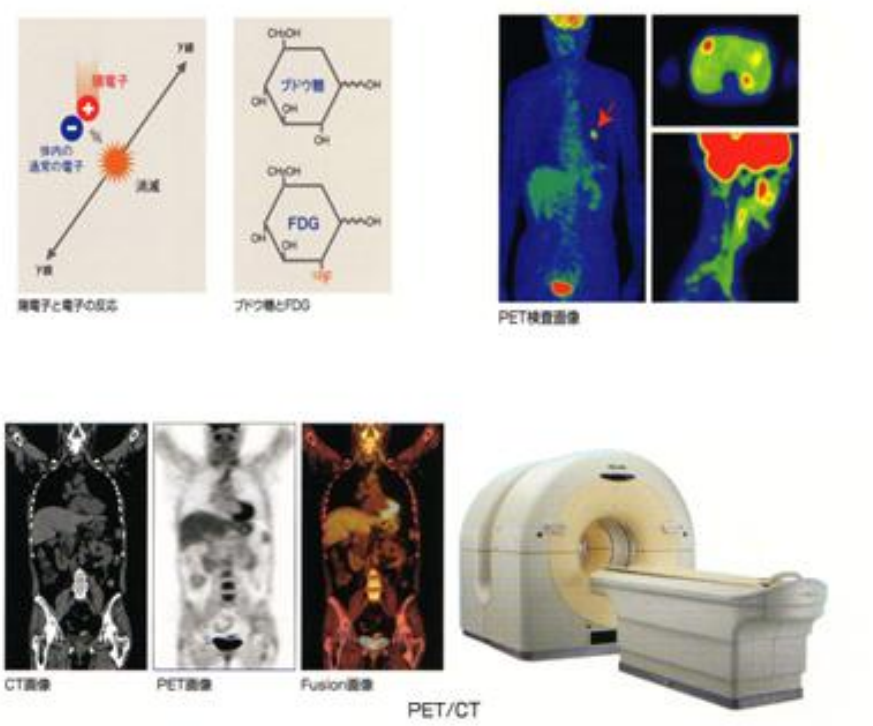
Positron-Emission Tomography and Assessment of Cancer Therapy

Malik E. Juweid, M.D., and Bruce D. Cheson, M.D.

POSITRON-EMISSION TOMOGRAPHY (PET) IS A NONINVASIVE IMAGING technique that exploits the unique decay physics of positron-emitting isotopes. The isotopes of oxygen, carbon, nitrogen, and fluorine have been used in the development of diagnostically useful biologic compounds that are available for PET imaging in order to provide a functional or metabolic assessment of normal tissues or disease conditions.

The past few years have seen a tremendous expansion of clinical applications of PET, particularly in oncology, mostly with the use of ^{18}F-fluorodeoxyglucose (^{18}F-FDG) as the PET tracer. PET with ^{18}F-FDG is now being used in the evaluation of several neoplasms, both before and after therapy, as well as in the planning of radiotherapy in various cancers, such as tumors of the lung and of the head and neck. Its use in the assessment of cancer after therapy, including restaging tumors and monitoring tumor response, is the focus of this article.

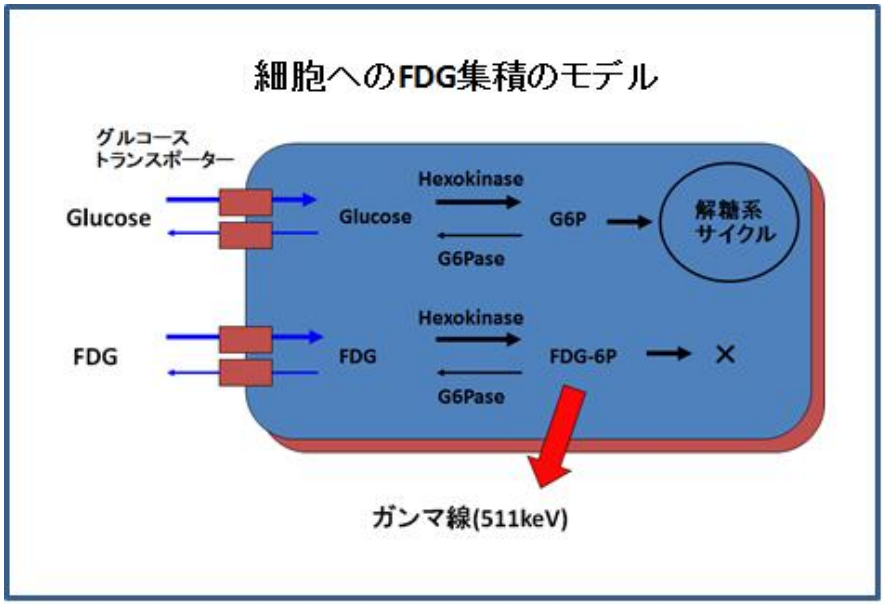
N Engl J Med. 2006 Feb 2;354(5):496-507.

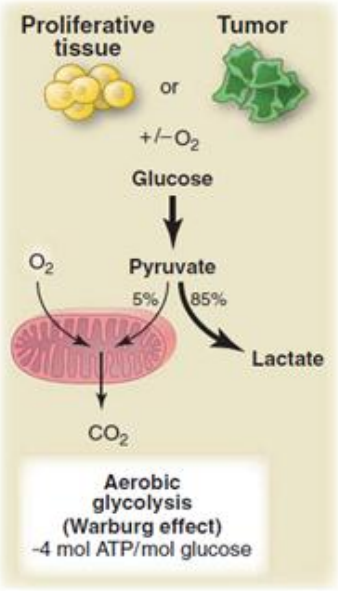


Positron Emission Tomography in Oncology

Warburg Effect and FDG PET

"The biological basis of FDG PET in oncology is the Warburg effect"





"Warburg Effect"
(Otto Warburg, 1924)

- Activation of glucose Metabolism

Aerobic Glycolysis

Metabolic requirements more than ATP

Vander Heiden et al. Science. 2009 May 22;324(5930):1029-33.

FDG取り込み能の半定量的指標：Standardized Uptake Value

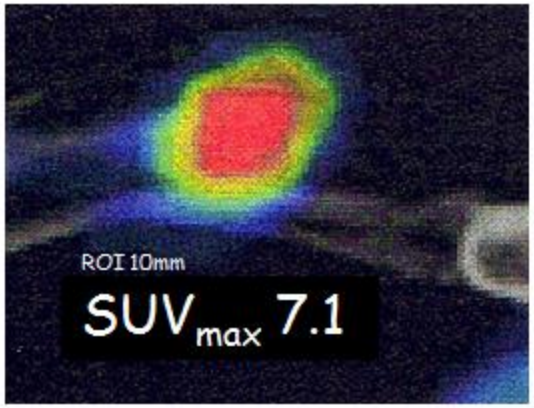
$$SUV = \frac{c(t)}{injected\ dose(t_0) \quad / \quad body\ weight}$$

c(t) = radioactivity concentration (MBq/kg) at time *t*

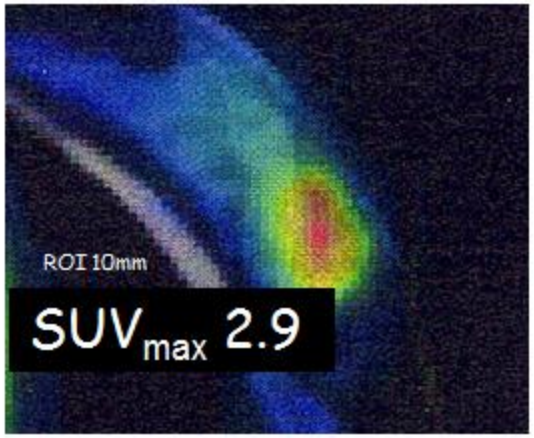
injected dose (e.g. in MBq) at the time of injection (*t*=0)

body weight (e.g. in kg).

Patient #1
67歳　乳がん
Size 2cm



Patient #2
65歳　乳がん
Size 2cm



t = 60min

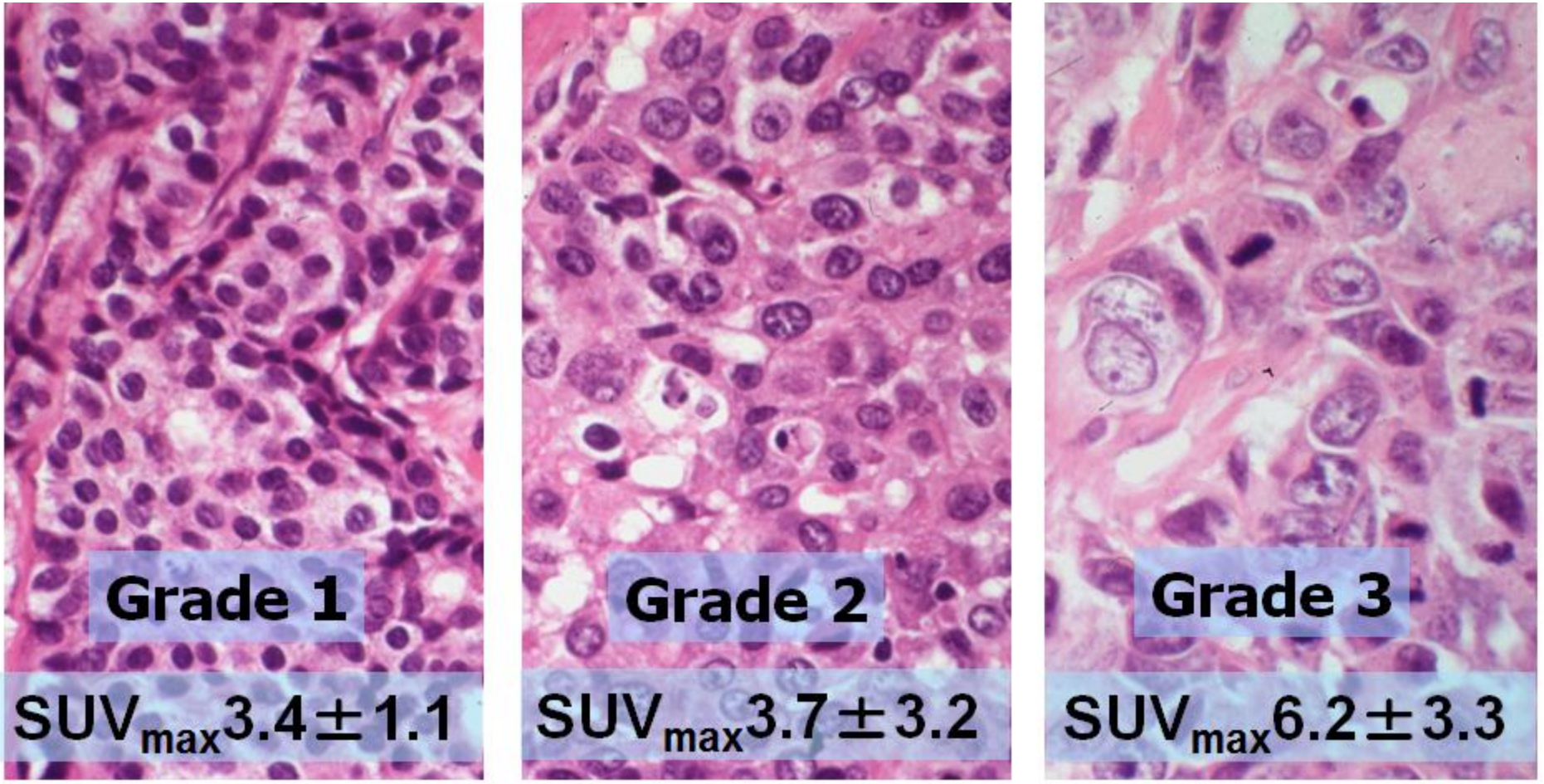
injected dose = 3.7 MBq/kg

原発性乳がん152症例の臨床病理学因子とSUVの相関

Variables	SUVとの相関	P value
年齢	≦ 45　vs.　46 ≦	0.9
組織型	ILC　<　IDC	0.03
浸潤径	≦ 2cm　<　2.1cm ≦	<0.0001
Grade	Grade1.2　<　Grade3	<0.0001
Mitosis	≦5/10HPF　<　6/10HPF≦	<0.0001
HR	+　<　−	0.006
HER2	0 − 2+　<　3+	0.03
腋窩リンパ節	転移なし　<　転移あり	0.03

S Ueda et al. Jpn J Clin Oncol. 2008 Apr;38(4):250-8.

浸潤性乳管癌の代表的組織像



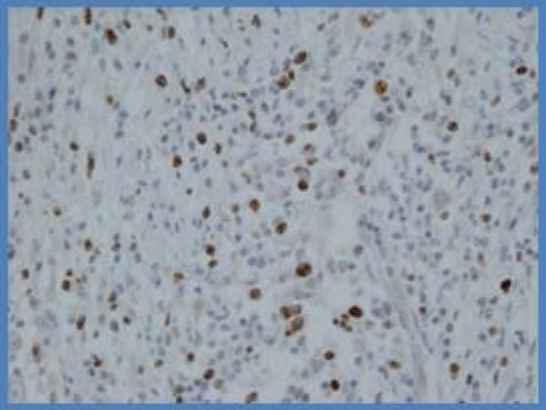
（腫瘍径2-3cmの乳がん65例）

Grade1/2 versus Grade3, $p < 0.0001$

S Ueda et al. Jpn J Clin Oncol. 2008 Apr;38(4):250-8.

免疫組織化学的検討

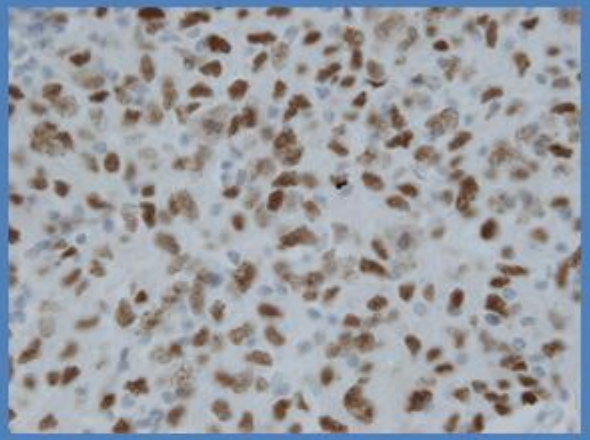
Ki67



Ki67	SUV_{max} 4>	4≦	
10% >	8	2	10
10% ≦	13	23	36
	21	25	46

P=0.01

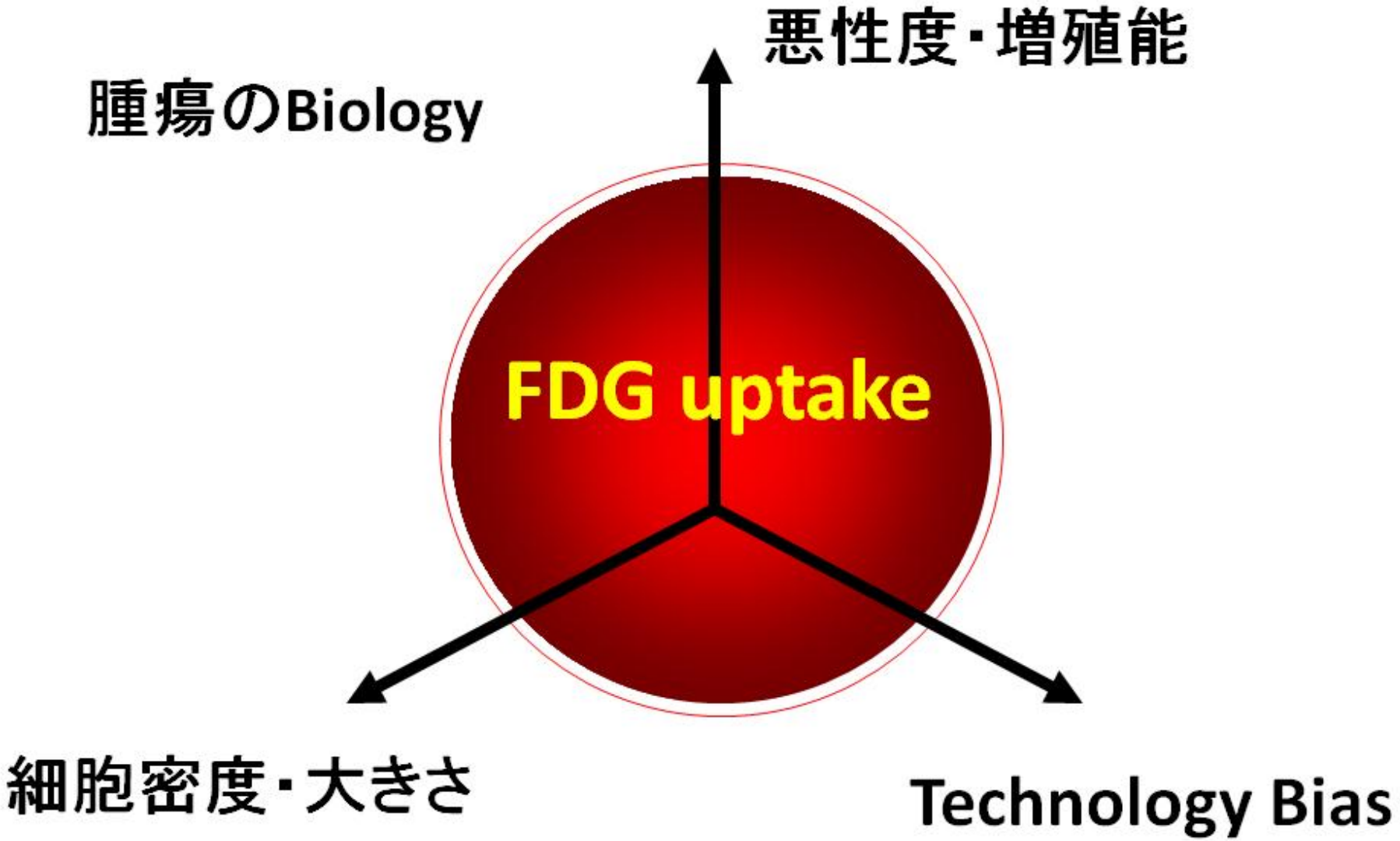
p53



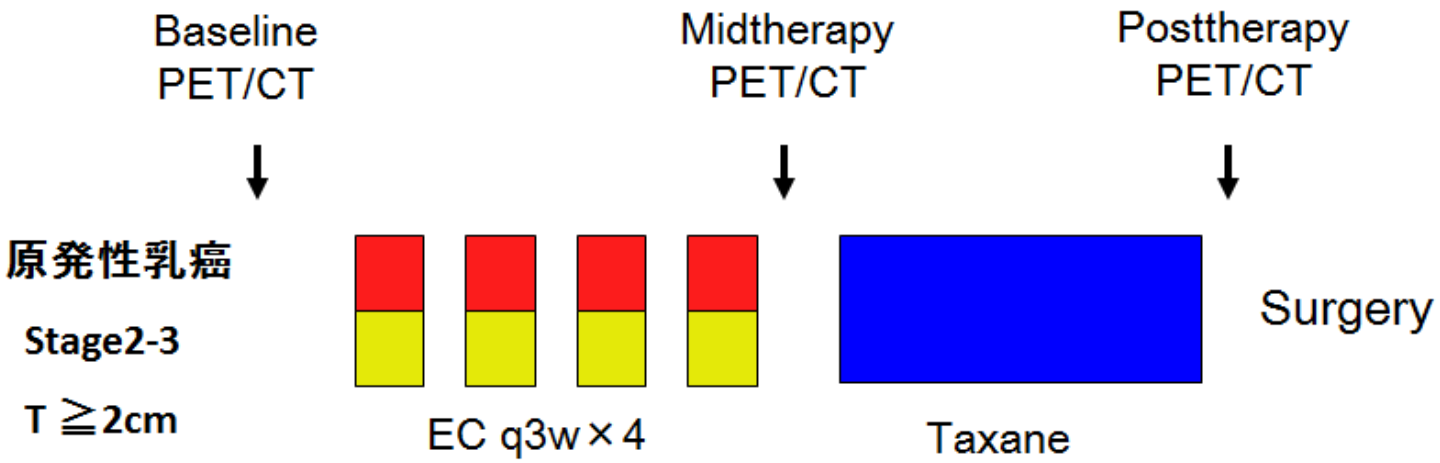
p53	SUV_{max} 4>	4≦	
1% >	19	17	36
1% ≦	2	9	11
	21	26	47

P=0.04

S Ueda, et al. BMC Cancer. 2008 Dec 22;8:384.


悪性度・増殖能
腫瘍のBiology
FDG uptake
細胞密度・大きさ
Technology Bias

臨床研究プロトコール



目的

2施設でFDG PETによる治療効果モニターリングの結果を比較し、最適な評価方法を検討する。

FDG-PET/CT

FDG 3.7MBq/kg, t = 60min, SUV最大値(SUVmax)

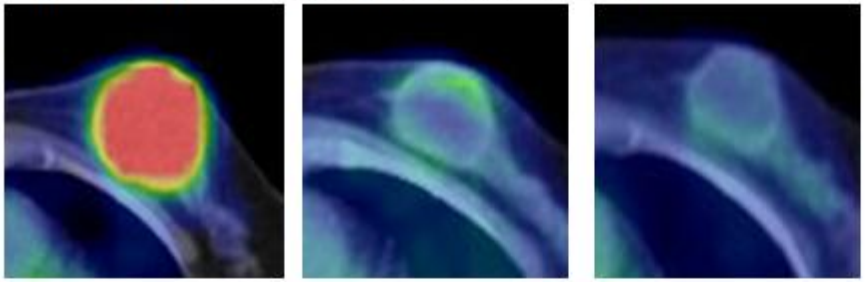
Endpoint

病理学的完全奏効率(pCR)

S Ueda et al, Int J Clin Oncol. 2011 Aug 10

pCR

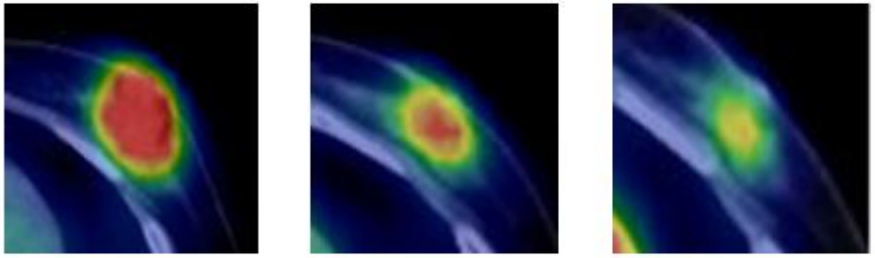
K.T., 71 y/o, Lt. IDC, Size 46mm, cN1,G3, ER+,PR+,HER2 0,
(Post therapeutic Pathologic Response Grade 3**)



SUV max6.13 DAY -14 | SUV max1.59 DAY 84 | SUV max1.14 DAY 179

PR

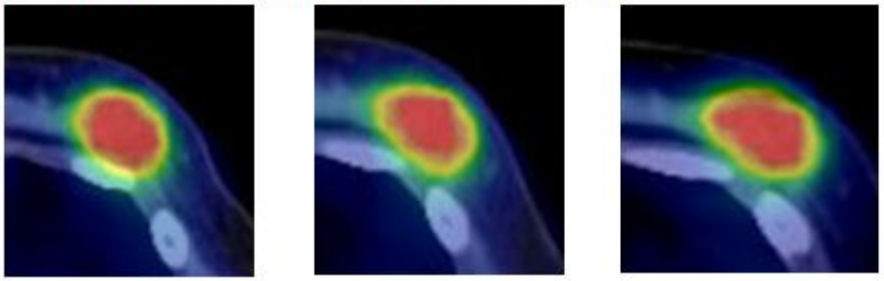
A.E., 67 y/o, Lt. IDC, Size 36mm, cN1,G1, ER+,PR+,HER2 1+,
(Post therapeutic Pathologic Response Grade 1a**)



SUV max7.01 DAY -7 | SUV max3.86 DAY 77 | SUV max2.59 DAY 158

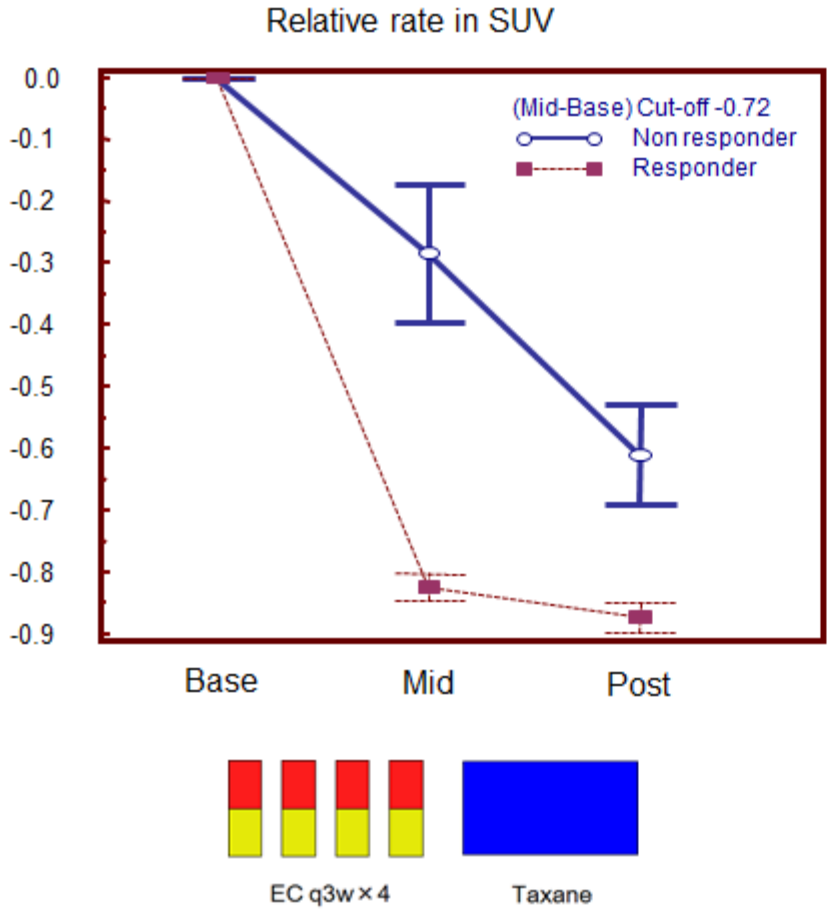
SD

A.E., 58 y/o, Rt. IDC, Size 40mm, cN0, G3, ER+,PR+,HER2 2+(FISH-),
(Post therapeutic Pathologic Response Grade 0**)



SUV max6.21 DAY -11 | SUV max5.11 DAY67 | SUV max5.09 DAY 121

S Ueda et al, Int J Clin Oncol. 2011 Aug 10



Overall (n = 98)

	non-pCR	pCR	Total (%)
NR	63	2	65 (66.3)
R	17	16	33 (33.7)
Total (%)	80 (81.6)	18 (18.4)	98

Sensitivity	88.90%
Specificity	78.80%
NPV	96.90%
PPV	48.50%

S Ueda et al, Int J Clin Oncol. 2011 Aug 10

まとめ

1. SUVは腫瘍の大きさや乳がんの増殖能・悪性度と相関する。
2. SUV変化率は、pCR予測の感度、特異度ともに良好であり、かつ施設間差が少ない。