Clinical Implication of PET

BIRC; Biomedical Research Institute

Takashi Kudo

Biomedical Imaging Research Center

"We promote basic and clinical research to provide the advancing medical practice by means of various approaches in radiological sciences, aiming to open the gates to the future through the peaceful use of nuclear energy and radiation."
Director of BIRC, Yasuhisa Fujibayashi.

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ポインタ 34° 43'57.37" N 131° 55'28.16" E

ストリーミング 99%

上空 1093.43 km

UNIV. OF FUKUI BIRC established in 1994

Why PET?

- PET (positron emission tomography)
  - Non-invasive and quantitative measurement (measurement with absolute unit)
    - Reason; PET measures not single photon emission, but coincidence of two photons from positron annihilation.
  - Suitable for measuring physiologic parameters.
    - Reason; Positron emitter includes essential nuclei such as N-13, O-15 and C-11. Using these nuclei, production of labeled material biologically identical to natural substrates (such as O-15 water) becomes possible.

Clinical Implication of PET

- Diagnosis of Ischemia (for patient with poor SPECT image)
  - Rb-82 PET imaging
- Evaluation of preclinical perfusion abnormality.
  - MBF and flow reserve measurement by N-13 Ammonia (or O-15 water) PET
- Viability assessment in ischemic heart disease
  - FDG PET (+ perfusion image) as a gold standard
- Studying non-ischemic heart dis.
  - Metabolic efficacy with C-11 acetate
  - Neurocardiology with C-11 HED
  - Flow reserve and endothelial function with N-13 acetate.
  - …etc, etc.

PET tracers

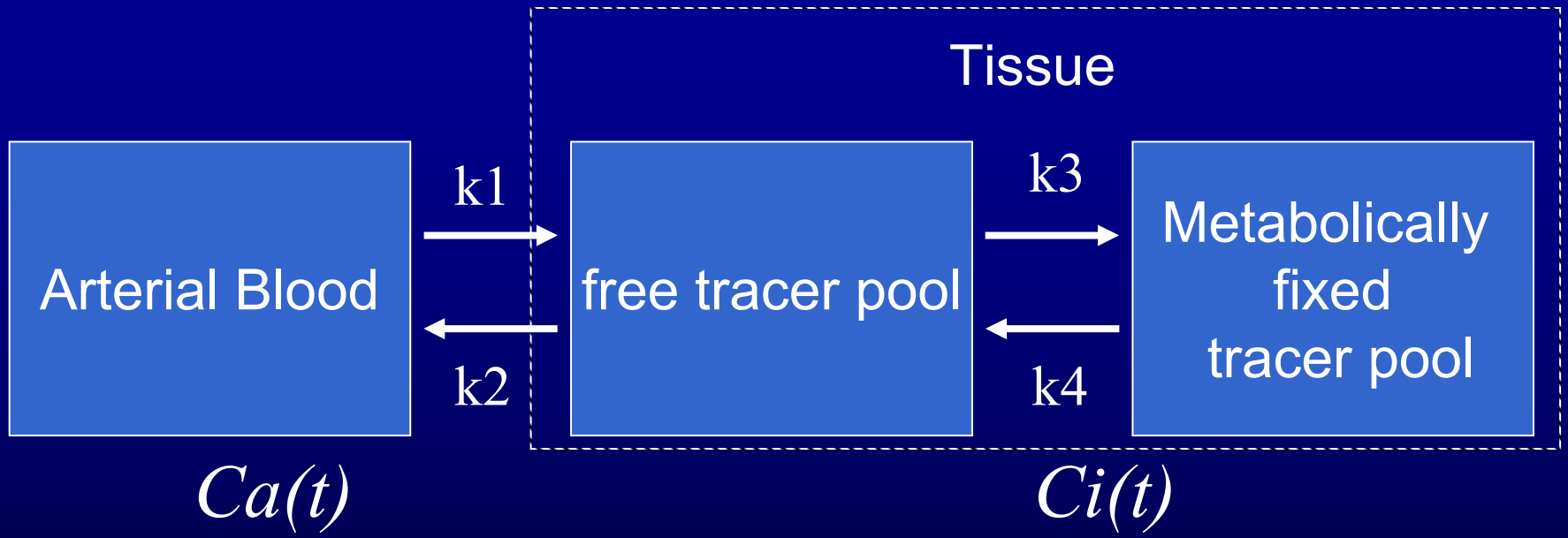
	Utility
• Perfusion	
– Trapped tracers	Flow Reserve (FR)
• N-13 Ammonia, Rubidium-82	
– Freely diffusable tracer	FR, Viability
• O-15 water	
• Metabolism	
– FDG; Glucose metabolism	Viability
– C-11 Acetate; Oxidative metabolism	Viability, Efficacy
• Neuroimaging	
– C-11 Hydroxyephedrine	Heart failure,
• Molecular Imaging	
– F-18 FES	Too Many….
– F-18 FHBG	Too Many….

N-13 NH_3;
Absolute measurement of perfusion.

Perfusion;
Flow reserve, Endothelial function.

- N-13 NH_3: Physiologically retained
  - High extraction fraction.
  - Metabolically trapped to the myocardium.
    - Consideration of activity and kinetic of metabolite is required
  - Simple static image; Relative perfusion
  - Parametric image; Quantitative perfusion.
- O-15 Water: Free diffusion
  - Freely diffusable between blood and myocardium.
  - Simple static image is not useful
    - Water distributes both to myocardium and to arterial blood. Thus, to visualize myocardium subtraction of blood activity is required.

Model for MBF (myocardial blood flow) measurement



- NH3 is metabolically trapped in myocardium (mainly as a form of glutamine).
- There are many mathematical model for MBF measurements. (2compartment, 3compartment with 2 parameters, 3 compartment with 4 parameters. etc. etc...)

How the N-13 NH_3 images are acquired…

Tracer Injection
(t=0min)

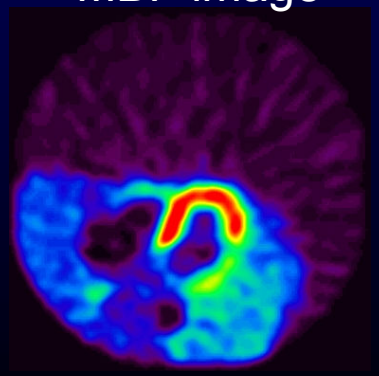
Transmission

Image acquired with external rotating rod source and without internal tracer. Purpose; attenuation correction. (For PET/CT, transmission scan is usually replaced with quick CT scanning)

Dynamic acquisition
(5min)

5 sec x 12 frames,
10 s. x 6 fr.,
20 s. x 3 fr.,
30s. x 4 fr.

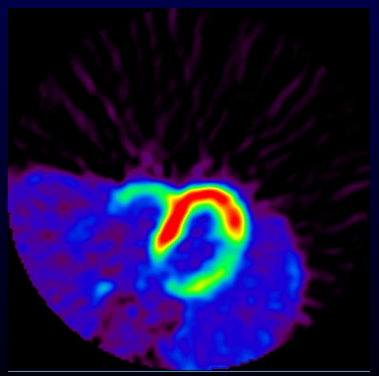
Parametric MBF image



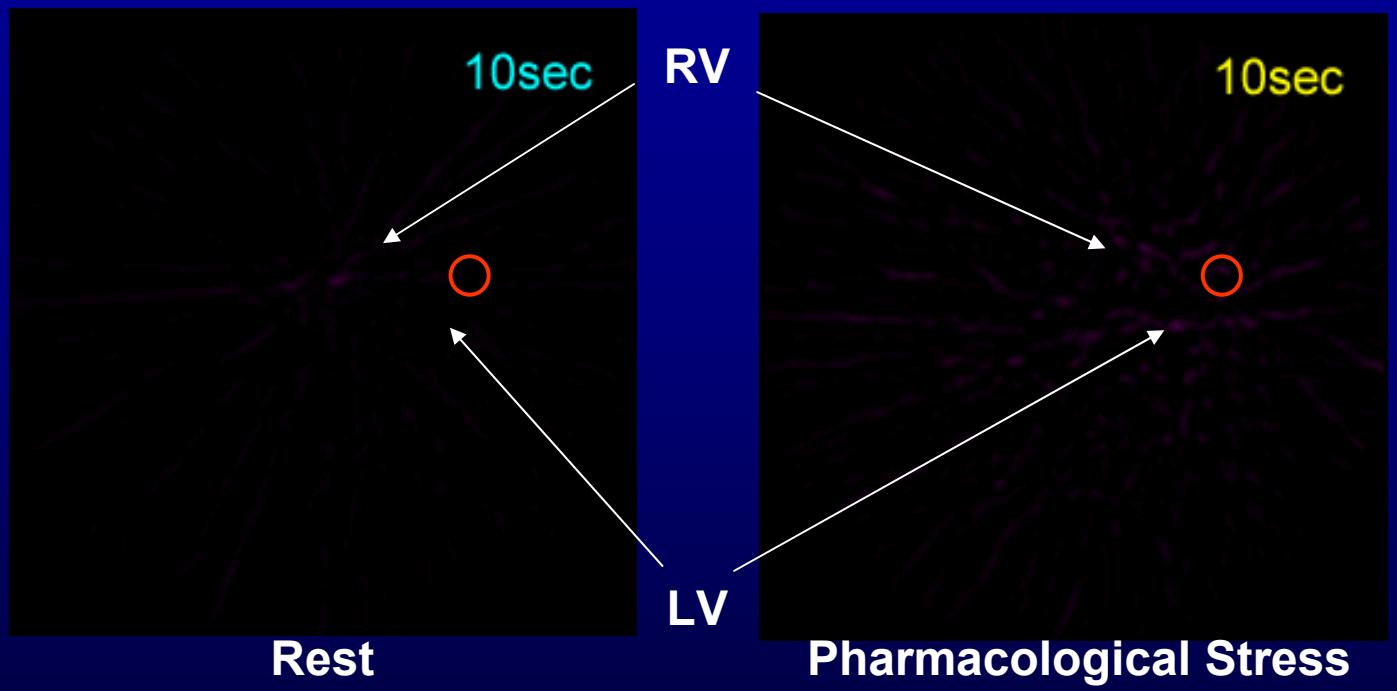
ECG gated acquisition
(10min)

(8~12 frame / cardiac cycle)

Relative perfusion distribution and cardiac function measurement.

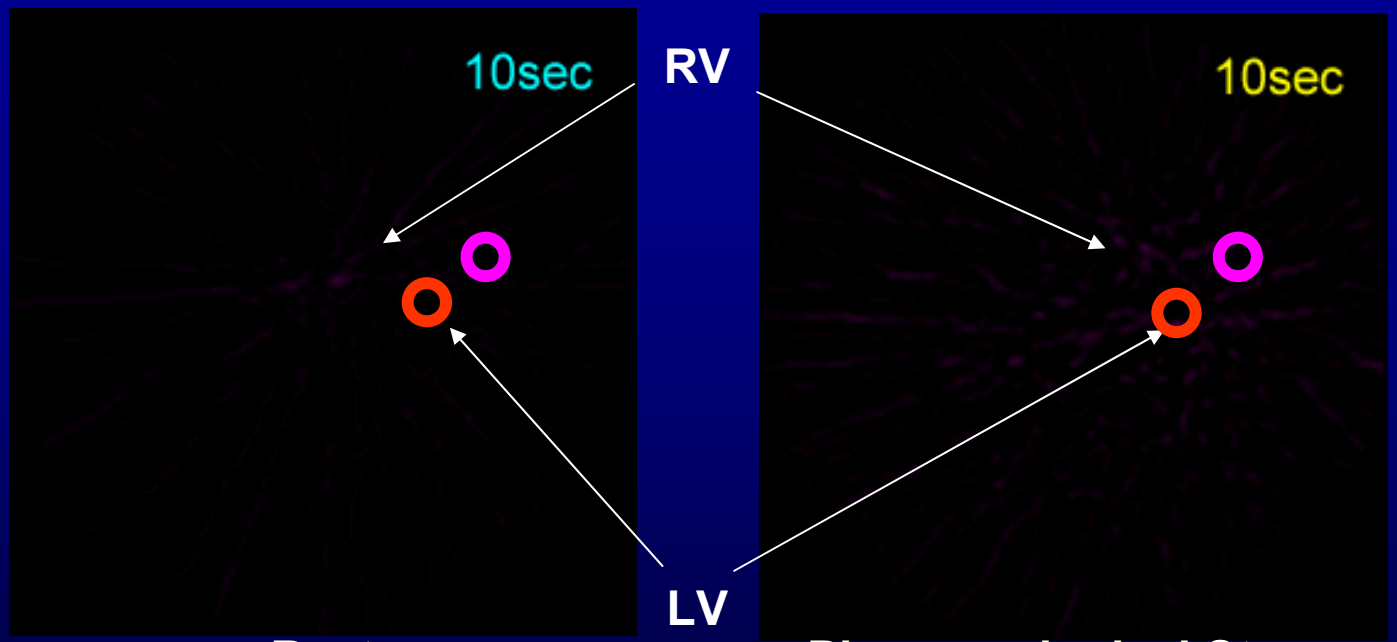


N-13 NH_3 PET is usually acquired with dynamic acquisition.



- Dynamic image over 5min.
- Note that the LV cavity size is larger in stress image.
  - Subendocardial ischemia is clearly visualized.

Dynamic acquisition is required for the quantitative MBF measurement.



- Quantitative measurement usually requires arterial blood count sampling. However, for the cardiac application, LV (or LA) cavity is clearly visualized an useful as arterial blood activity. (Everything we need is in the image.)

$$\frac{Ci(t)}{Ca(t)} = k^* \frac{\int_0^t Ca(\tau)d\tau}{Ca(t)} + \frac{MBF^2 V}{(MBF + k_3)^2} + f_b \frac{AB(t)}{Ca(t)}$$

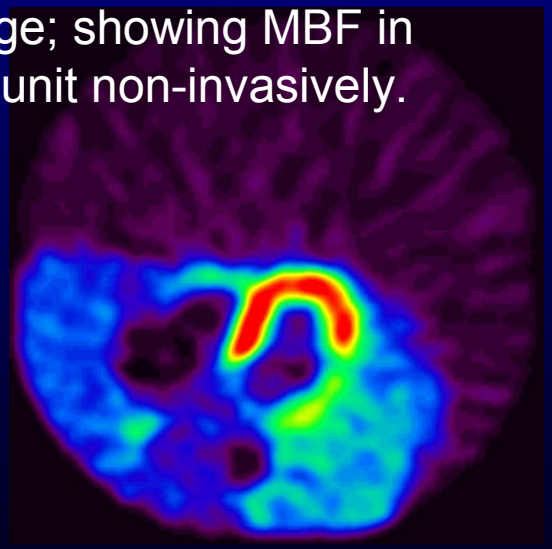
MBF measurement using Patlak graphical analysis method

$$\frac{Ci(t)}{Ca(t)} = k^* \frac{\int_0^t Ca(\tau)d\tau}{Ca(t)} + \frac{MBF^2 V}{(MBF + k_3)^2} + f_b \frac{AB(t)}{Ca(t)}$$

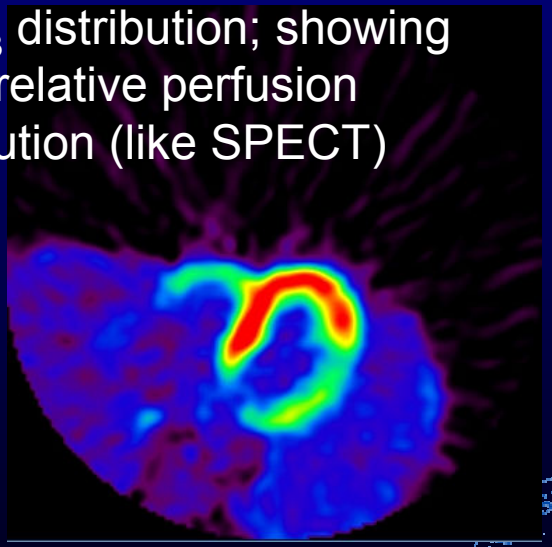
$$k^* = 1 - 0.607 e^{(-1.25/MBF)}$$

- Solving these two equations, we can calculate MBF

MBF image; showing MBF in absolute unit non-invasively.



N-13 NH_3 distribution; showing only relative perfusion distribution (like SPECT)



Only PET can visualize MBF in absolute unit as a image.

Why absolute measurement is important?

- Requirement for future cardiology
  - Finding preclinical ischemia/microvascular damage, abnormality in vasomotor function before significant CAD/ACS.
  - Treating severely ill patients such as ischemic cardiomyopathy or severe heart failure after advanced therapeutic intervention (including DES, CRT, gene therapy, etc.....)

To study and follow up these conditions, relative perfusion image analyzed with SPECT is totally not enough.

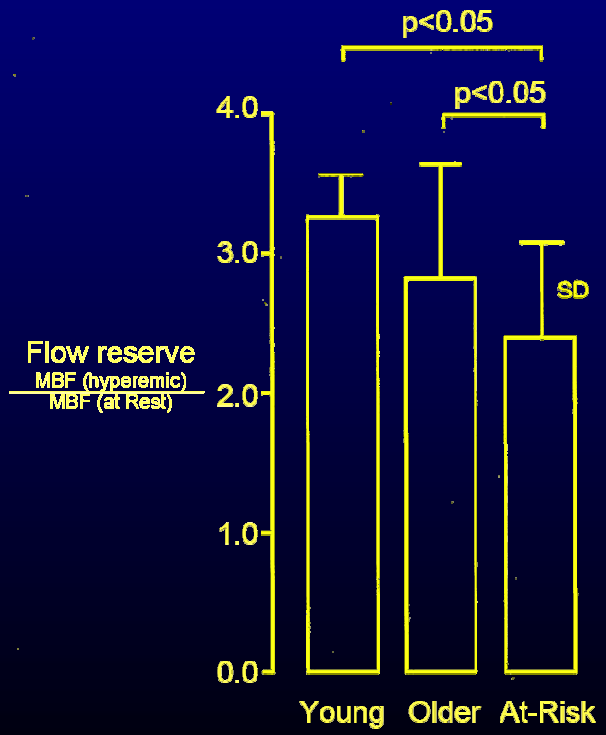
- There are many researches which indicate the flow reserve and/or endothelial function is impaired with risk factors, preclinical condition such as...
  - Smoking
    - Campisi R et.al., Circulation (1998) 98: p119
  - Hypercholesterolemia
    - Yokoyama I et.al., Circulation (1996) 94: p3232
  - Diabetes, insulin resistance.
    - Schindler TH et.al., J Am Coll Cardiol (2006) 47: p1188
  - ...etc, etc.

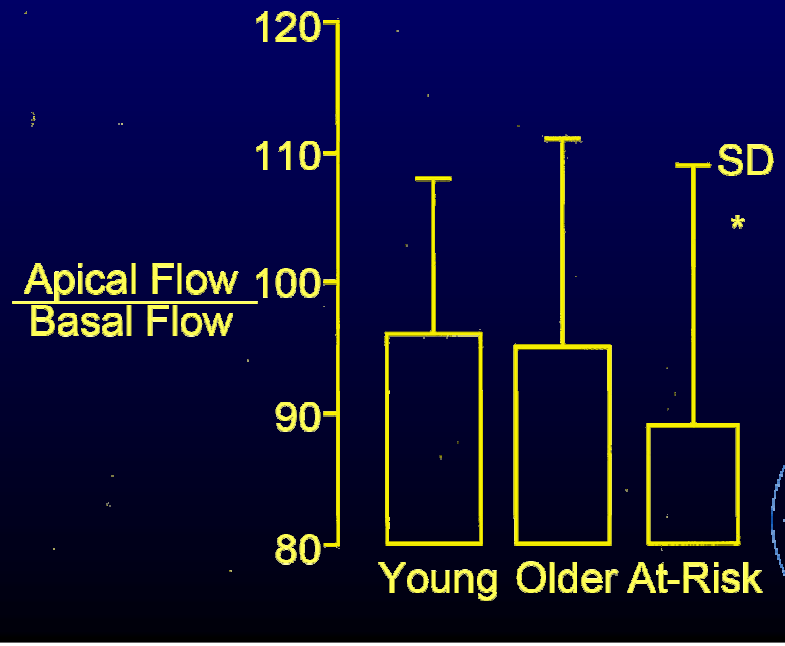
Example; Longitudinal flow gradient
(flow in apical side < basal side)

- Pampaloni M.H., et.al. Circulation (2001) 104:p527~
  - Young volunteer (around 25 y.o.), Old Volunteer (around 55 y.o.) and Pt. with coronary risk factor without coronary stenosis (around 53y.o.) were compared.

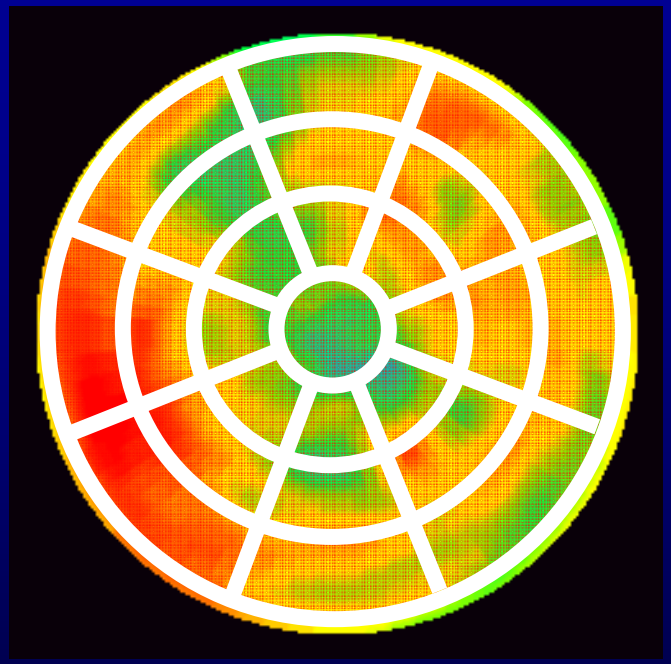
Example; Longitudinal flow gradient

- Flow reserve (=Max. hyperemic MBF/ rest MBF) is reduced in patient with risk factor but even old person without risk showed slight reduction in flow reserve.
- On the other hand, significant longitudinal flow gradient (MBF on apical myocardium/MBF on basal myocardium) was only found in patient with risk, not in old normal volunteer.





Coronary perfusion steal



Apical; 28

Mid; 21

Basal; 15

- 120 consecutive chronic CAD patients are analyzed retrospectively.
- Myocardium was divided into 24 segments (apex was excluded) and number of segments which showed steal (defined as "hyperemic MBF<rest MBF") was analyzed.
- Steal tend to found more frequently in apical side than basal myocardium.

Message

- In the future cardiology, information of relative perfusion distribution may not enough for evaluation of patients.
- N-13 ammonia PET (and other perfusion PET imaging) can provide important information about absolute myocardial blood flow.
- Practically, only PET can provide such kind of quantitative measurement of MBF.

FDG;
Gold standard of viability assessment

Metabolism; Viability assessment

- Concept
  - Ischemic myocardium preferentially uses glucose. (Metabolic switch)
  - Viable myocardium has relatively maintained metabolism compared with decreased perfusion. (Flow/metabolism Mismatch)
- Tracer
  - FDG; for glucose metabolism
  - C-11 acetate; for oxidative metabolism.

FDG PET; gold standard of viability

☆Present situation (in Japan);

- Nobody argue with the fact that FDG is well known, evidence proven gold standard for viability assessment.
- However, growth of FDG PET application to cardiology is not good as we expected.

There are sky-rocketing growth of FDG PET market for oncologic application.
Why not for cardiac application?

FDG; gold standard for viability

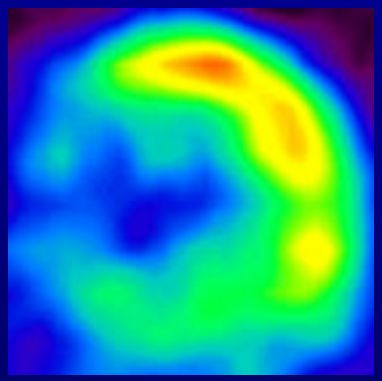
- High sensitivity, Specificity, NPV, PPV
  - No uptake of FDG=No metabolism, No living tissue, Not viable

	Sensitivity	Specificity	
Tillisch J. et al., NEJM 1986; 314. p884	95	80	Glucose load
Tamaki N. et al., Am J Cardiol. 1989; 64. p860	78	78	Fasting

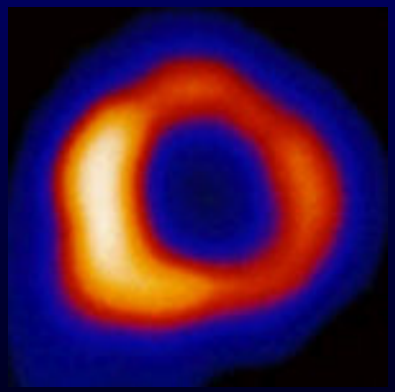
- However….>>AHA/ACC/ASNC guideline; Class I, Level of Evidence B
  - Method (patient preparation, image interpretation, diagnostic criteria, etc.) is not clearly standardized.
  - ASNC guideline.

Two way of patient preparation.

Fasting

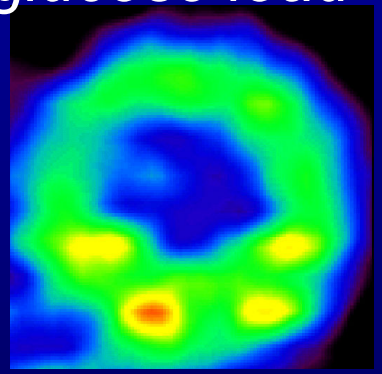


F-18 FDG

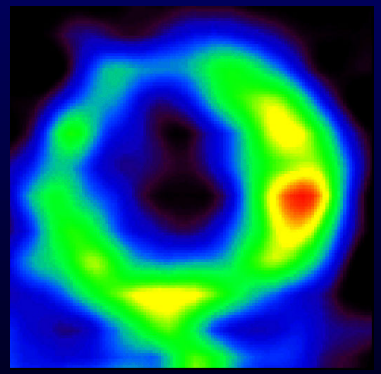


Perfusion
(Tl SPECT)

Oral glucose load



F-18 FDG

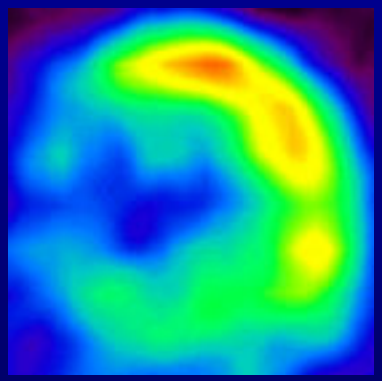


Perfusion
(NH_3 PET)

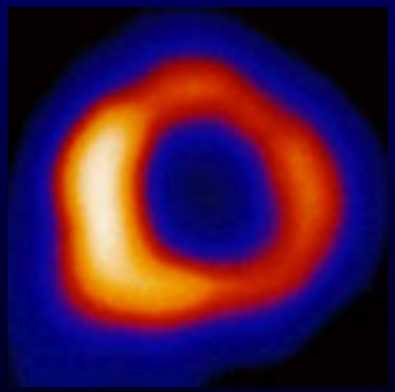
- Fasting
  - Normal myocardium mainly uses fatty acid and FDG uptake is low. Ischemic myocardium has enhanced glycolysis and uptakes FDG prominently.
- Glucose load
  - Normal myocardium shows enhanced glucose utilization. Damaged but viable myocardium shows relatively maintained glucose utilization and FDG uptake.

Two way of patient preparation.

Fasting

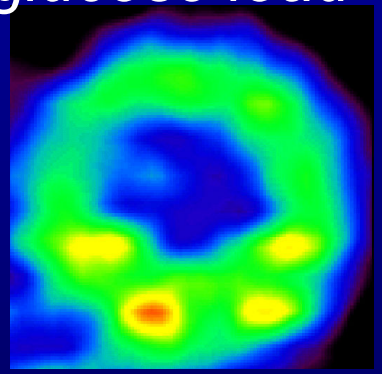


F-18 FDG

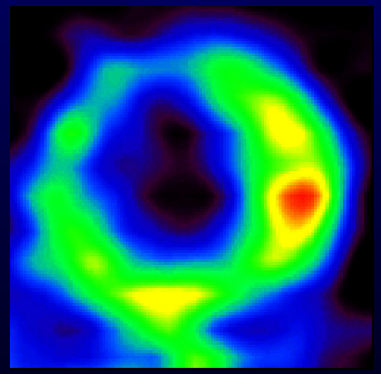


Perfusion
(Tl SPECT)

Oral glucose load



F-18 FDG

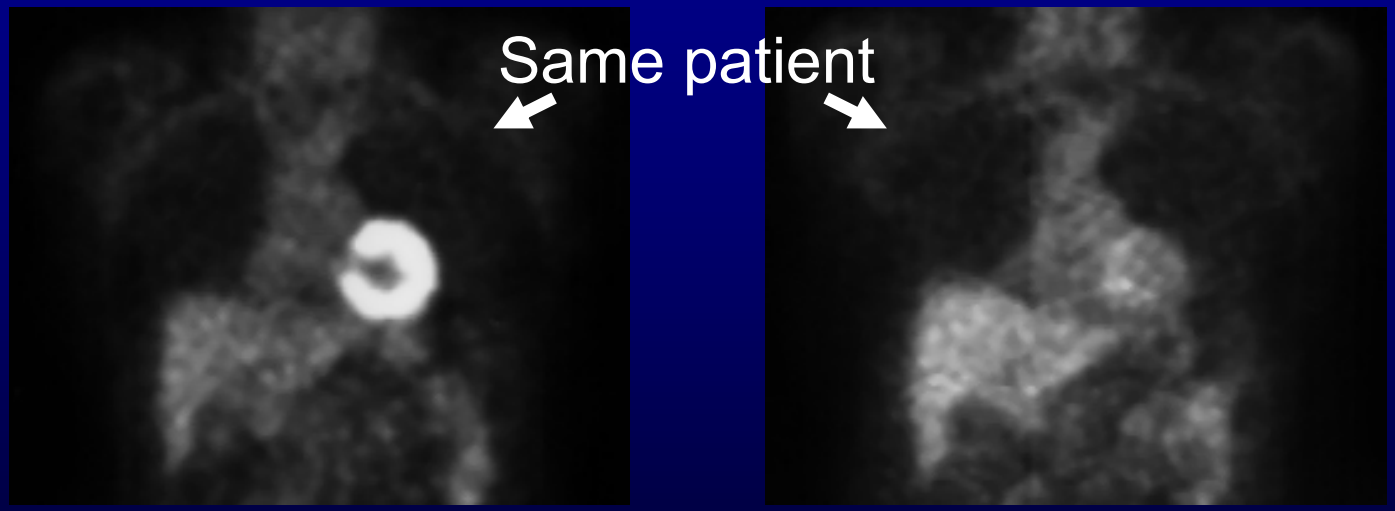


Perfusion
(NH_3 PET)

- If everything goes well, viable myocardium will be visualized as “hot image”.
- To make FDG uptake in normal myocardial minimal, special effort (overnight fasting, heparin injection etc.) is required.
- Even with such efforts, good image quality is not always achieved.

FDG PET; influence of metabolic milieu.

- I (PET nuclear cardiologist) previously learned that normal myocardium under fasting condition shows negative FDG uptake (with few exception).



Blood sugar 98mg/dl Fasting duration 4hr.

Blood sugar 106mg/dl Fasting duration 8hr.

- Now, with help of large body of experience with oncologic PET performed under fasting condition, we know regulation of FDG uptake is quite complex.

FDG; Preparation

- Standard is oral glucose load
  - Oral glucose load
    - Take glucose (about 75g) orally. Scan is performed 40-60 later.
    - Problem; High blood sugar level reads to poor image.
  - Insulin clump
    - Using continuous infusion of insulin and glucose, stabilize blood sugar level below 150mg/dl. Then iv FDG.
    - Problem; complexity of method.
  - Compromised method
    - Using look up table and measured blood glucose level, insulin is injected.
    - Problem; There is no standardized look up table for insulin dose/glucose level.
  - FAA lowering drug (Nicotinic acid derivative)
    - Acipimox is usually used
    - Problem; only available in Europe.

ASNC guideline; Journal of Nuclear Cardiology, 10; p543~

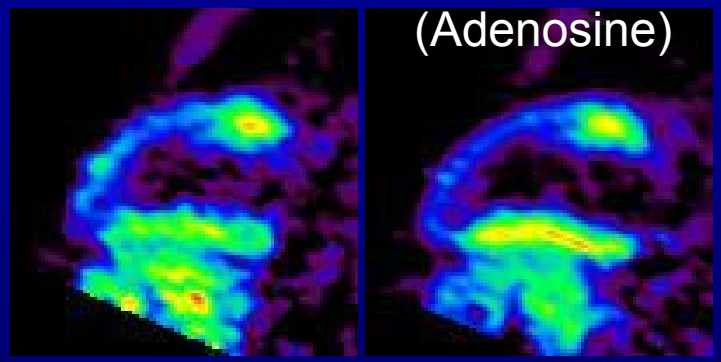
- Fasting image; Not included in ASNC guideline

Case

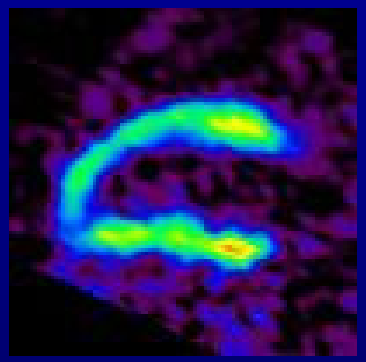
N-13 ammonia (perfusion)

Rest

Stress (Adenosine)



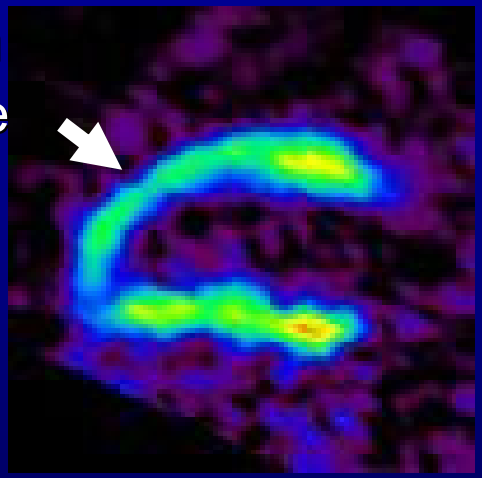
FDG (glucose load)



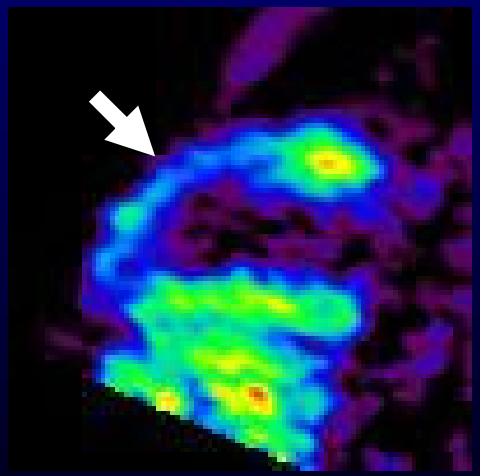
- 49yo male. AMI.
- Day 2 (about 24hr after onset);
  - PCI was performed for #6=100%. PCI for #6 was success, but #8=100%(thrombs) was found after #8 thrombectomy was unsuccessful.
- Day 10
  - N-13 ammonia PET (rest, stress); Anterior low perfusion with ischemia.
- Day 12
  - FDG PET (glucose load.); Anterior wall mild low uptake. % uptake of ant wall= around 50%
- Later CAG revealed distal LAD thrombs was disappeared after thrombolytic therapy.
- Echo at the time of PET; Ant, Lat, Septum= severe hypokinesis. LVEF=49%
- Echo on 7month later; Ant, Septum=hypokinesis. LVEF=63%

FDG PET; How to interpret

- 1) Flow/metabolism Mismatch
  - Always requires perfusion image
- 2) % Uptake of FDG
  - Requires FDG image only.
    - Ratio to normal area (%uptake) >50~60%
- 3) Metabolic rate of glucose
  - Absolute measurement of metabolism
    - Threshold is around 0.25μmol/min/g
    - Large inter-individual variability requires some normalization.



FDG
(oral glucose load)



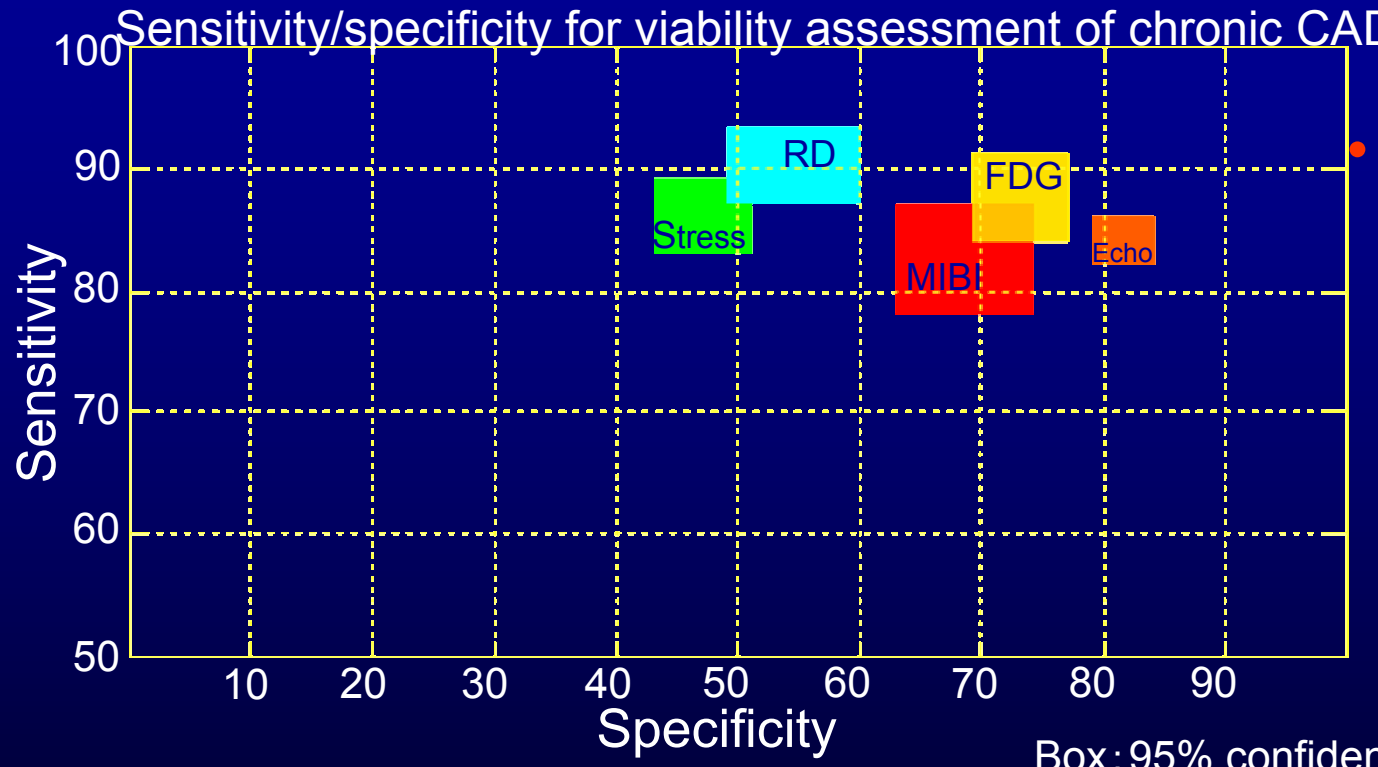
N-13 NH_3 PET
(Perfusion image)

Why FDG PET does not spread as we (only I?) expected?

- Methodological standard is not clear.
- Complex influence of metabolic milieu
  - Diabetic patients; Hard to study with FDG PET.
- Requirement of perfusion image
  - FDG PET is not stand alone.

- SPECT IS ENOUGH.
  - Oncology; With FDG PET, clinical staging may change in 10% (or more) patients. (=10% misdiagnosis without PET)
  - Cardiology; How about IHD diagnosis??

The most important question; Is FDG-PET superior over SPECT



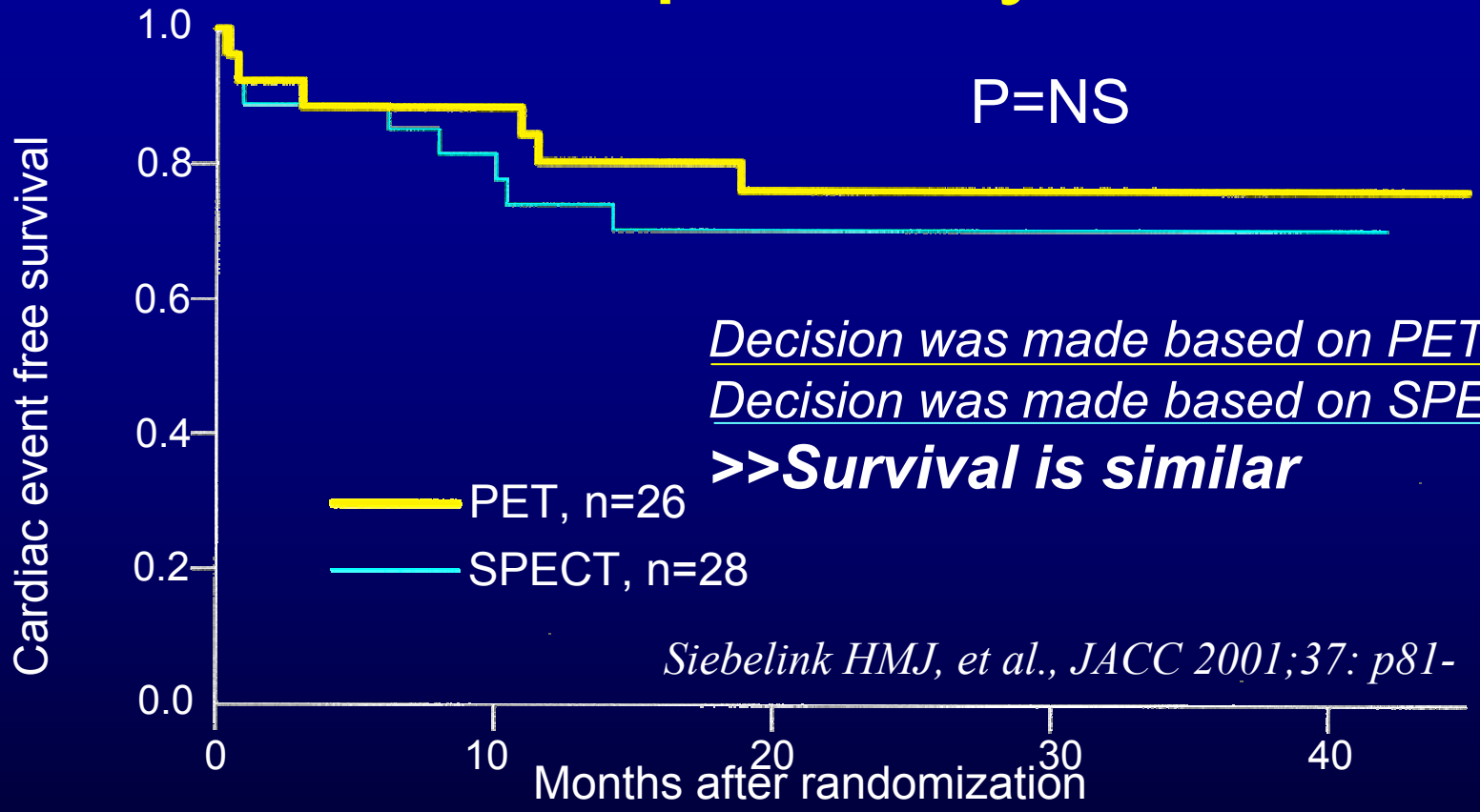
Box；95% confidence interval

- LD dob Echo
- FDG PET
- MIBI
- Tl Rest-RD
- Tl Stress-RD-reinjection

Regarding sensitivity and specificity, FDG PET is better than MIBI SPECT for viability assessment.

Bax JJ., et al. JACC 1997; 30: p1451-1460

FDG PET; Superiority over SPECT



Decision was made based on PET

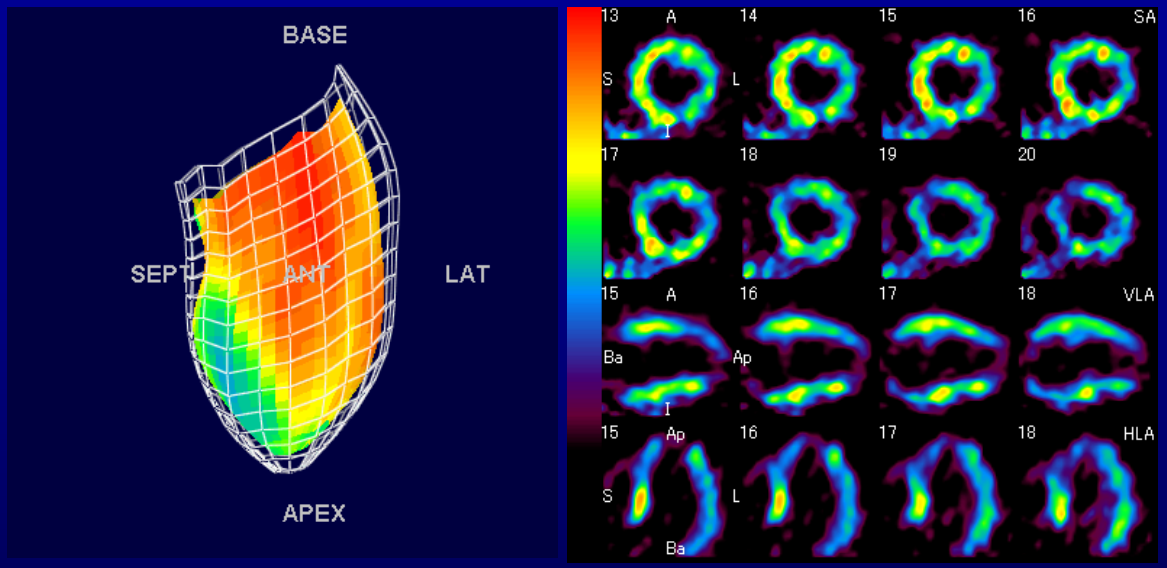
Decision was made based on SPECT (MIBI)

>>Survival is similar

Siebelink HMJ, et al., JACC 2001;37: p81-

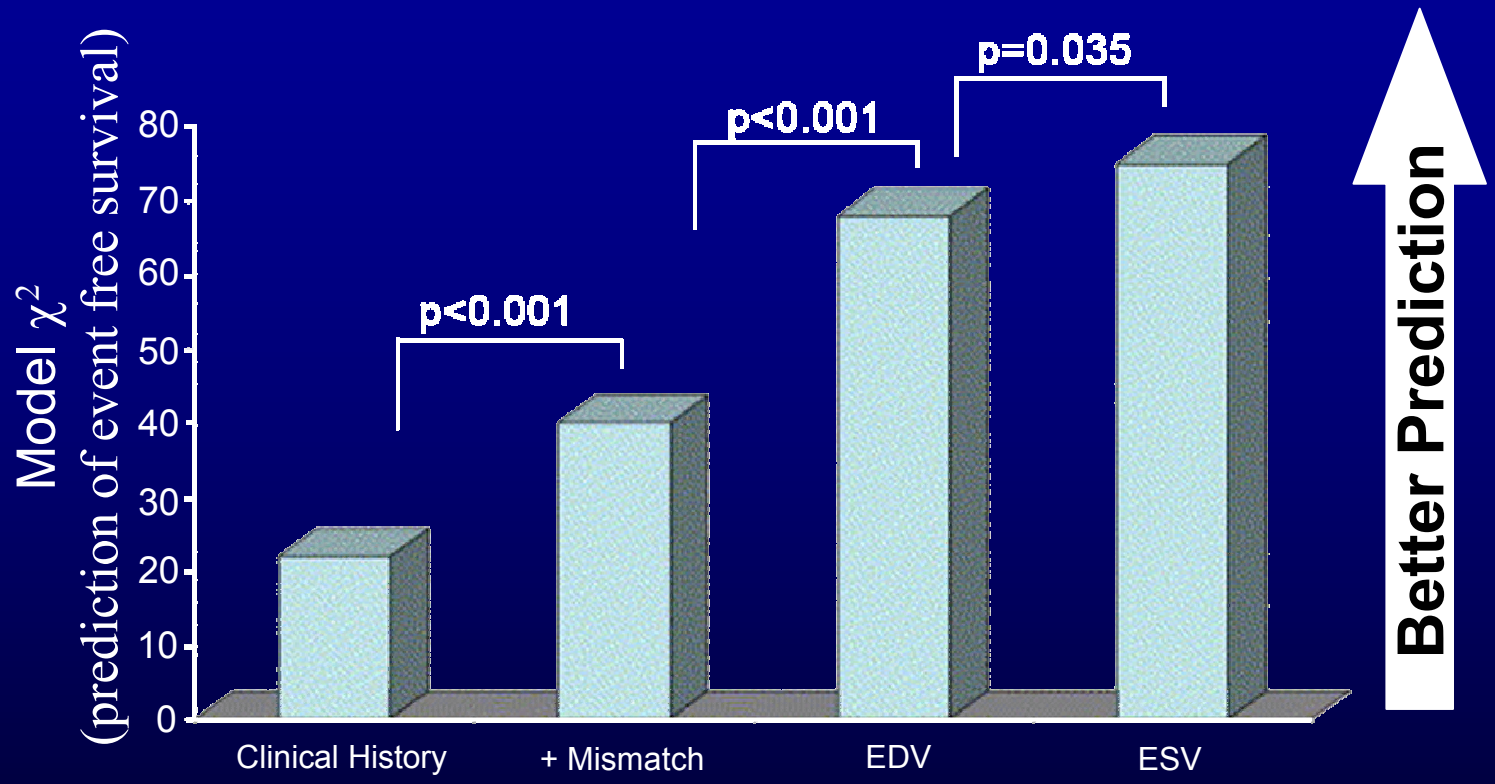
- No superiority for PET was found.
- My opinion
  - There is superiority, but the magnitude is small.
  - SPECT read by expert will performs excellent.

Let's make FDG PET more reliable!



- Introducing ECG gated SPECT technique into PET
  - Problem; No software (QGS, 4D-MSPECT, etc) provides official supports for use in PET.
    - All the auto/semi-automatic gated SPECT analysis programs are optimized for SPECT use.
    - Large difference of spatial resolution between PET and SPECT may make acquired value, especially volume value, unreliable one.

Gated FDG PET; Incremental value.



Santana CA et.al., J Nucl Cardiol 2004; 11: p542-

- Adding cardiac function parameters obtained with ECG-gate, FDG PET can more accurately predict outcome.

Summary

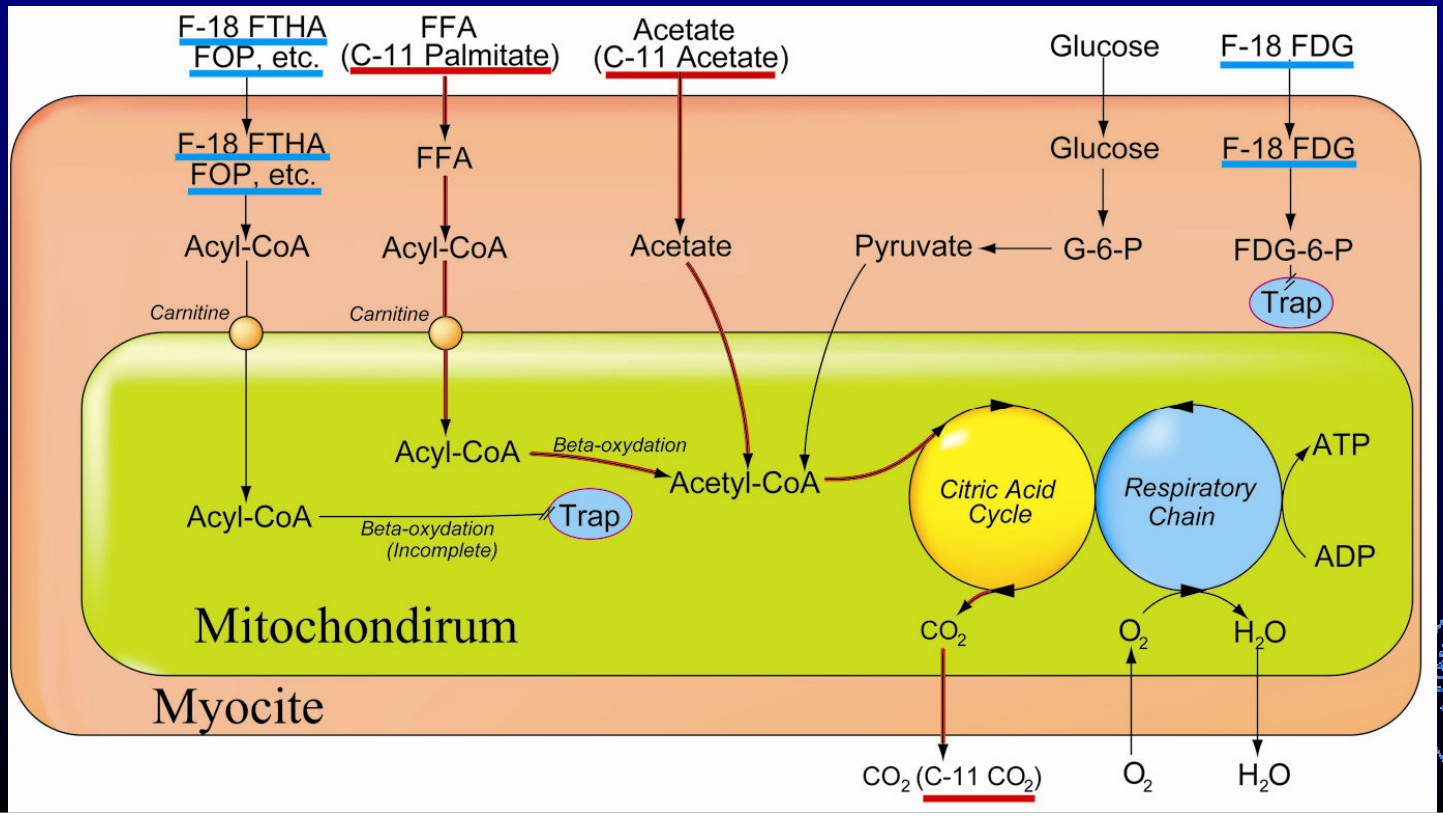
- FDG is well known tracer as gold standard of viability.
- However, the superiority over SPECT is not so significant.
- Lack of standardized method and difficult tracer character according to influence of metabolic milieu is big problem.

C-11 Acetate; All-in-one tracer.

Is there any better tracers?

C-11 Acetate; oxidative metabolism

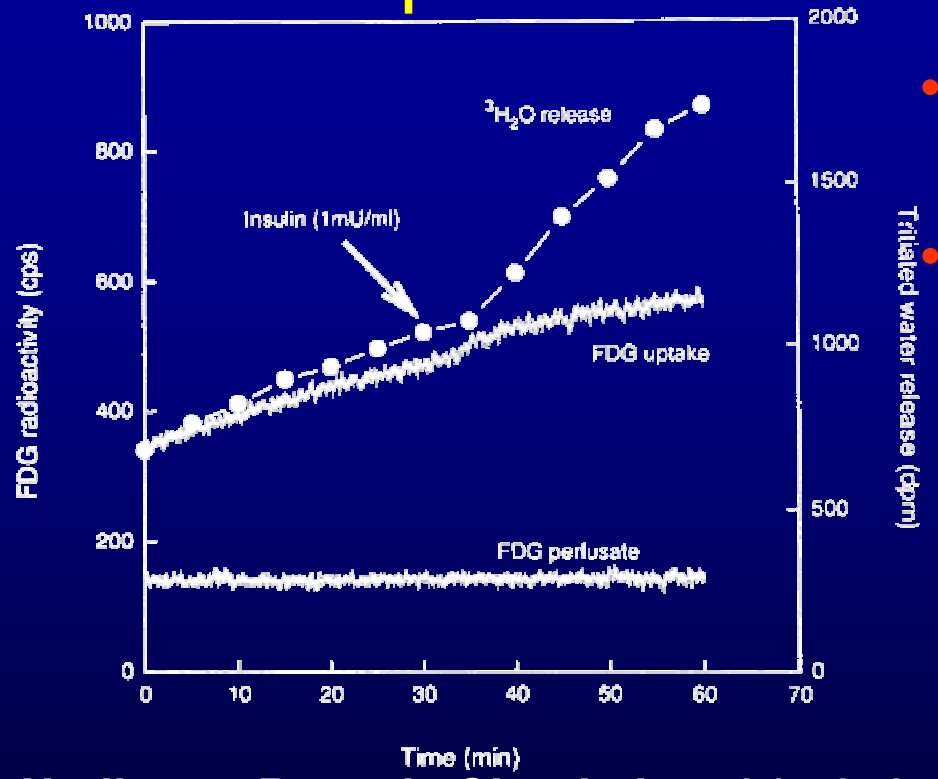
- Glucose metabolism is hard target.
  - Influence of metabolic milieu is too large and complex.
- Evaluation of TCA cycle: More easy target.
  - It lies on the end of the metabolic stream.
  - Influence of metabolic milieu is small.



Trapped tracer vs. metabolized tracer.

- Metabolized tracer; C-11 acetate.
  - Good
    - Truly physiological; Biologically equal to the circulating acetate.
  - Bad
    - Metabolized tracer usually requires dynamic data acquisition.
- Metabolically trapped tracer; FDG
  - Good
    - High image quality; Stable enough to acquire over several minutes.
    - Easy to analyze; Simple uptake usually reflects metabolic activity.
  - Bad
    - Not purely physiological tracer. It is not equal to circulating glucose.
    - Lumped constant may change according to metabolic condition (such as insulin level).
      - Lumped constant; Correction factor that equates FDG uptake to glucose uptake.

Lumped constant (LC);
problem with trapped tracer.



Hariharan R, et.al., Circulation; 91 p2435-

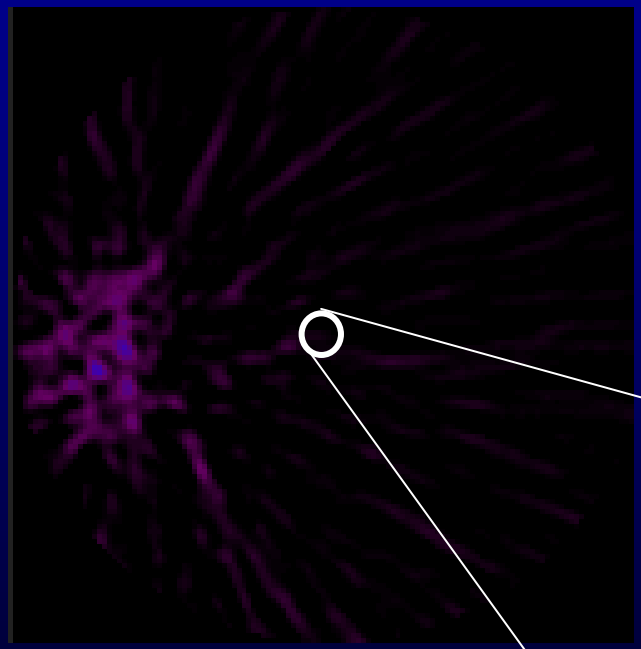
- A study with isolated rat heart
- FDG uptake and glucose metabolism (as tritium labeled water release) were compared.
  - After insulin administration, relation between glucose metabolism and FDG uptake was changed.

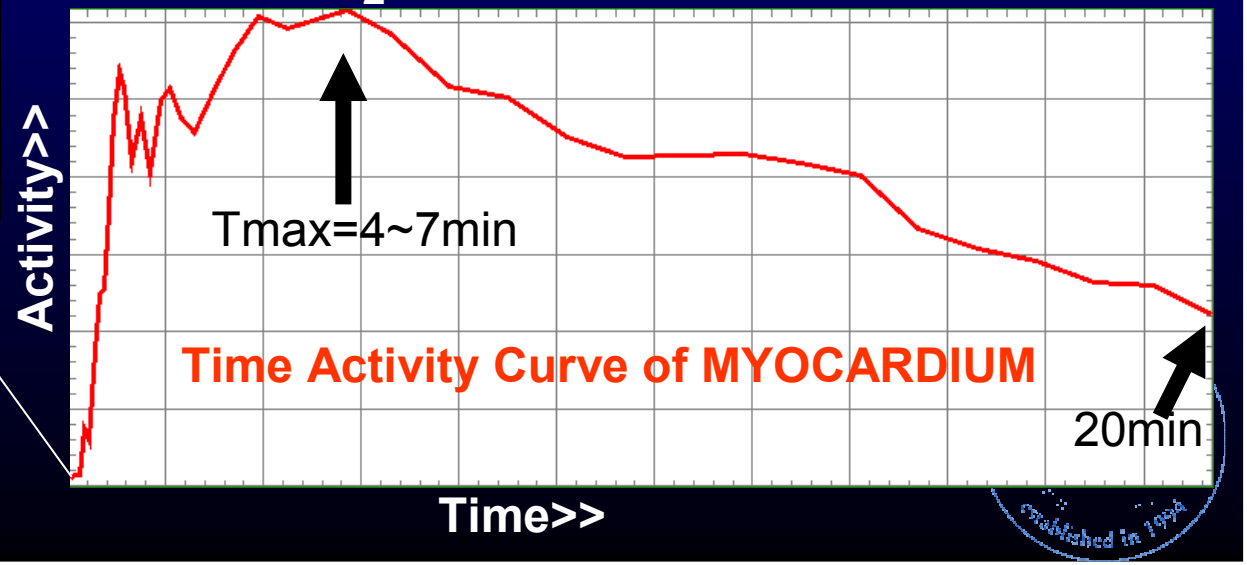
LC is not a CONSTANT,
it is a VARIABLE.

- FDG uptake gives us only rough assumption of glucose metabolism, although it is clinically acceptable.

Tracer kinetics of C-11 Acetate

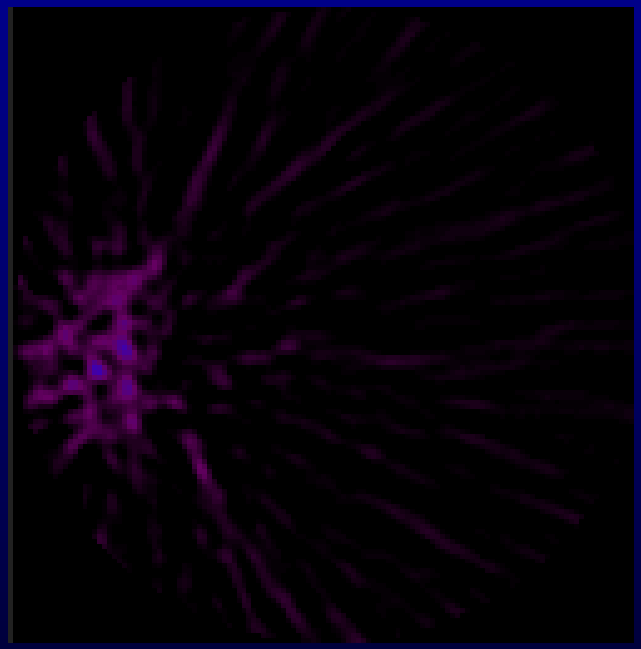
- Injected C-11 acetate rapidly distributes to the myocardium.
  - The early uptake correlate with myocardial perfusion. Thus, the early phase uptake is also useful as relative perfusion.
- Then, C-11 acetate is washout from myocardium as a form of C-11 CO_2





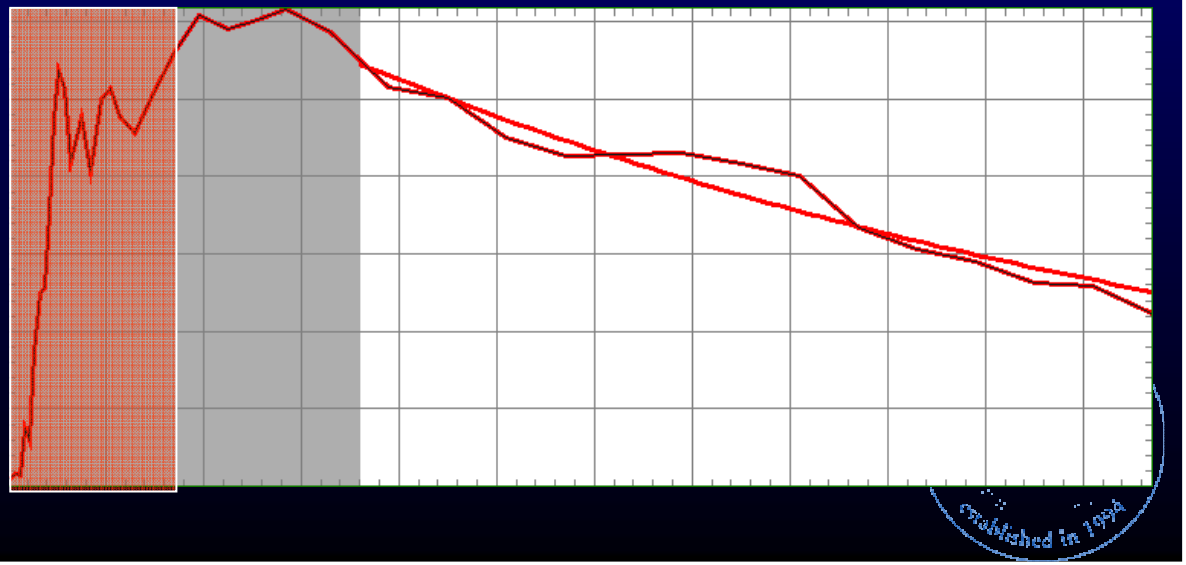
Kmono

- The time activity curve is divided into three phase.
- Washout rate constant (k) is calculated applying monoexpornential curve fitting to washout phase.



$$y=ae^{-kt}$$

It is usually called k_{mono}, and known to correlate with oxidative metabolism of myocardium.

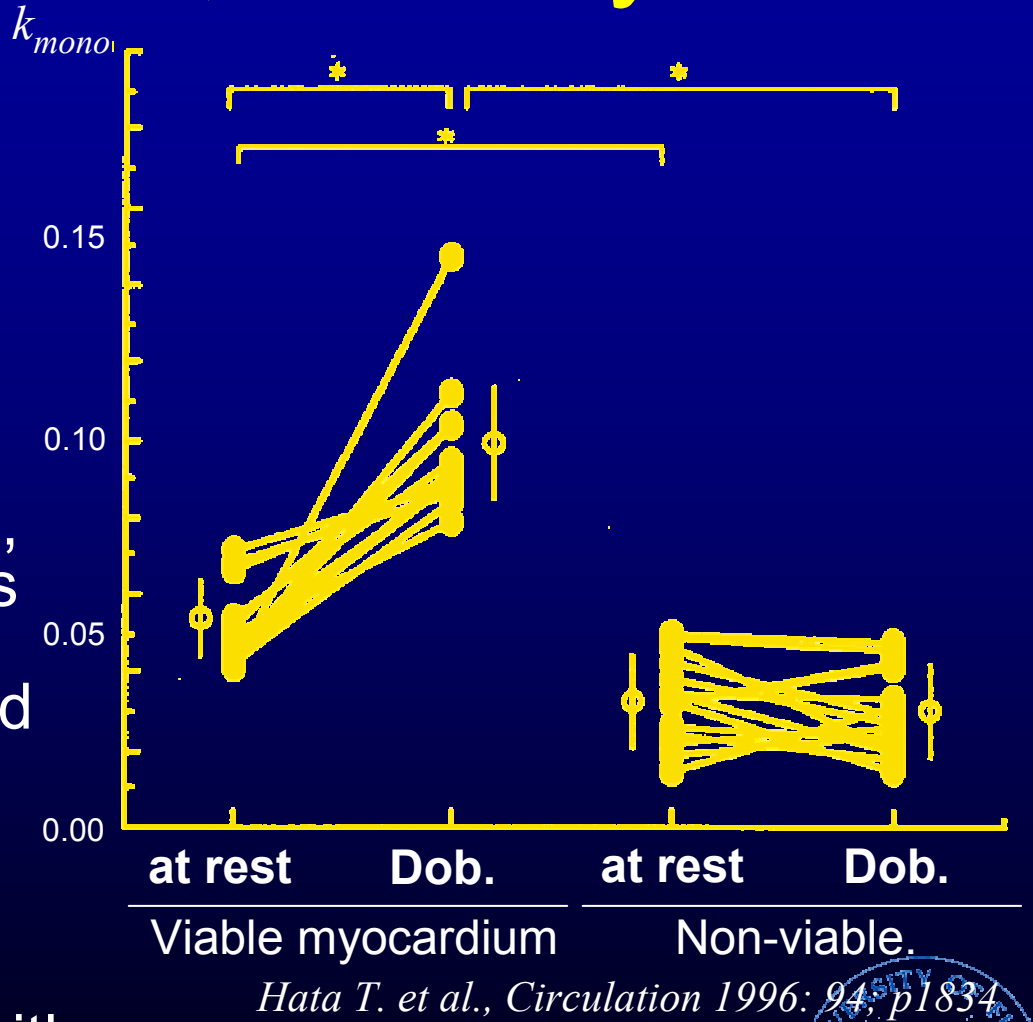


Input Phase (1~3min)
Peak (3-8min)
Washout phase(8min~

Acetate PET; Viability

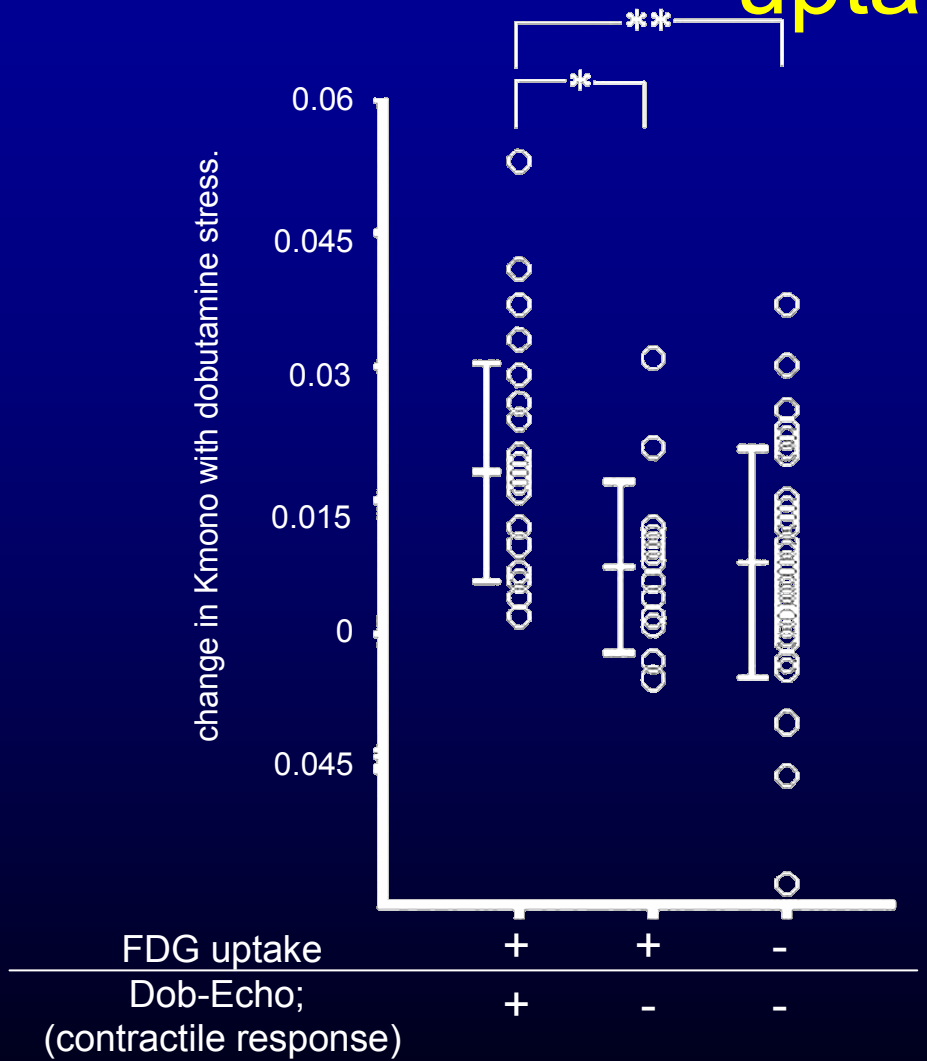
- Viable myocardium showed maintained k_{mono} value.
- However, k_{mono} shows overlap between viable and non-viable myocardium.
- Under dobutamine stress, viable myocardium shows acceleration of oxidative metabolism and increased k_{mono}. Non-viable myocardium does not.
- No overlap

Viability can be assessed with C-11 acetate PET.



Hata T. et al., Circulation 1996: 94; p1834

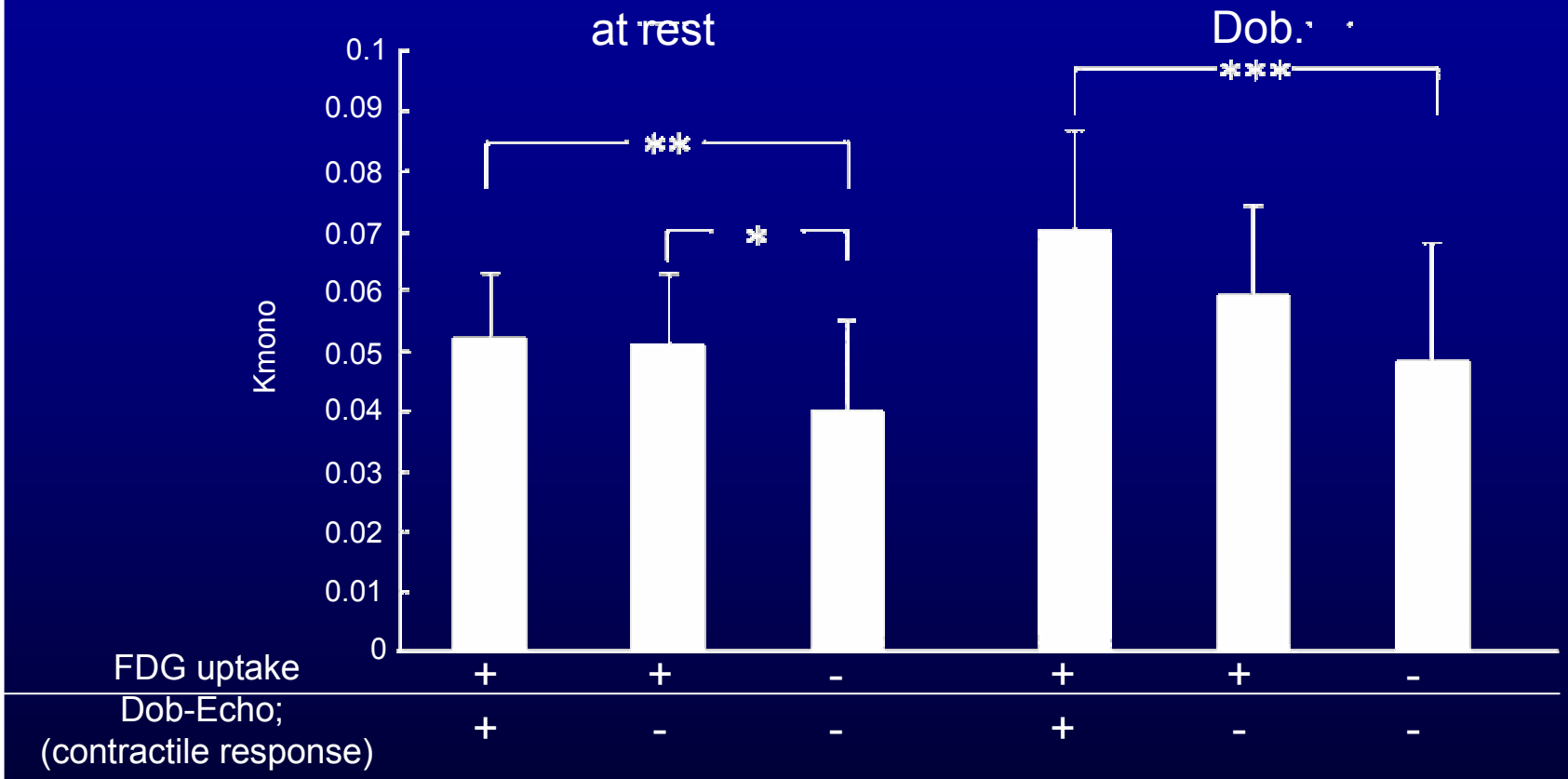
k_{mono}, Dobutamine stress, and FDG uptake



Yoshinaga et al. *J Nucl Med 2004; 45: p1885-*

- Comparison between FDG uptake, k_{mono} (at rest and dob), and dobutamine Echo.
  - There is significant number of segment which does not show contractile response to dobutamine stress but shows FDG uptake.
  - In such segments, metabolic response (change of k_{mono} with dobutamine stress) is poor.
- Metabolic response = contractile response?

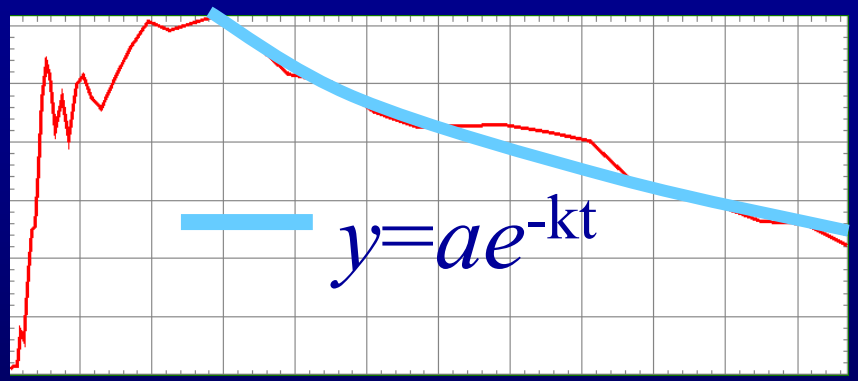
k_{mono}, Dobutamine stress, and FDG uptake

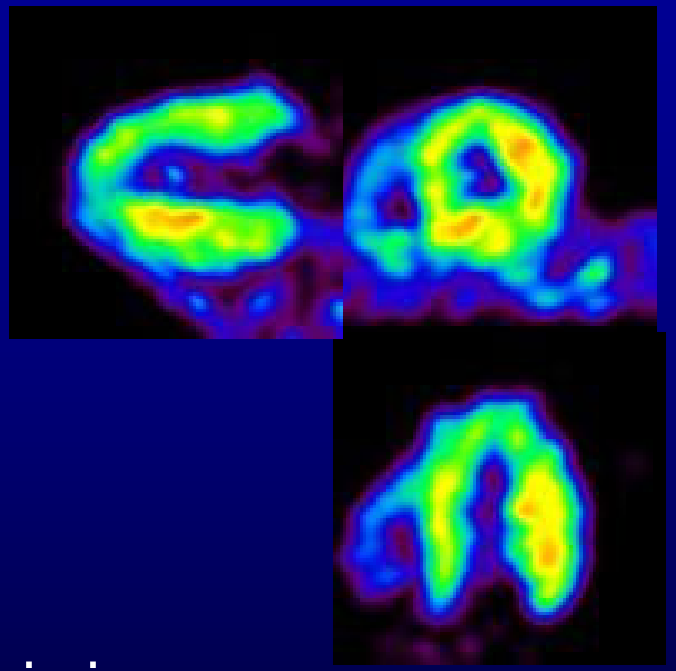


- k_{mono} measured at rest can be used as an equivalent of FDG uptake.

FDG uptake is IMAGE, Kmono is NUMBER.
IMAGE is always more easy to use than NUMBER

k_{mono} parametric image



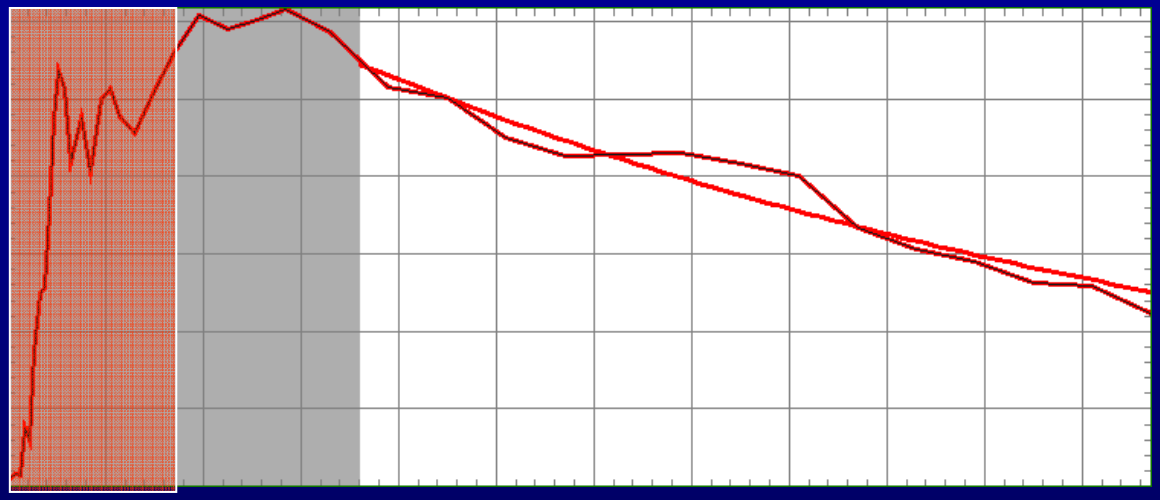


- Preliminary result of k_{mono} parametric image.
- k_{mono} can be calculated pixel by pixel manner. With this k_{mono} image, C-11 acetate PET may become equally useful as FDG PET not only for study use but also for clinical diagnosis.

Benefits of C-11 Acetate over FDG

- Less metabolic milieu influence
  - Kmono is not (or nearly not) influenced by the metabolic circumstances such as blood sugar, FAA, and insulin.
    - No need to worry about DIABETES.
- Perfusion information is available.
  - Early phase (about 3~7min after injection) tracer distribution correlates with myocardial perfusion distribution.
  - No need to perform another perfusion imaging.
    - One single C-11 Acetate PET can provide both relative perfusion and metabolic information.

C-11 acetate for perfusion



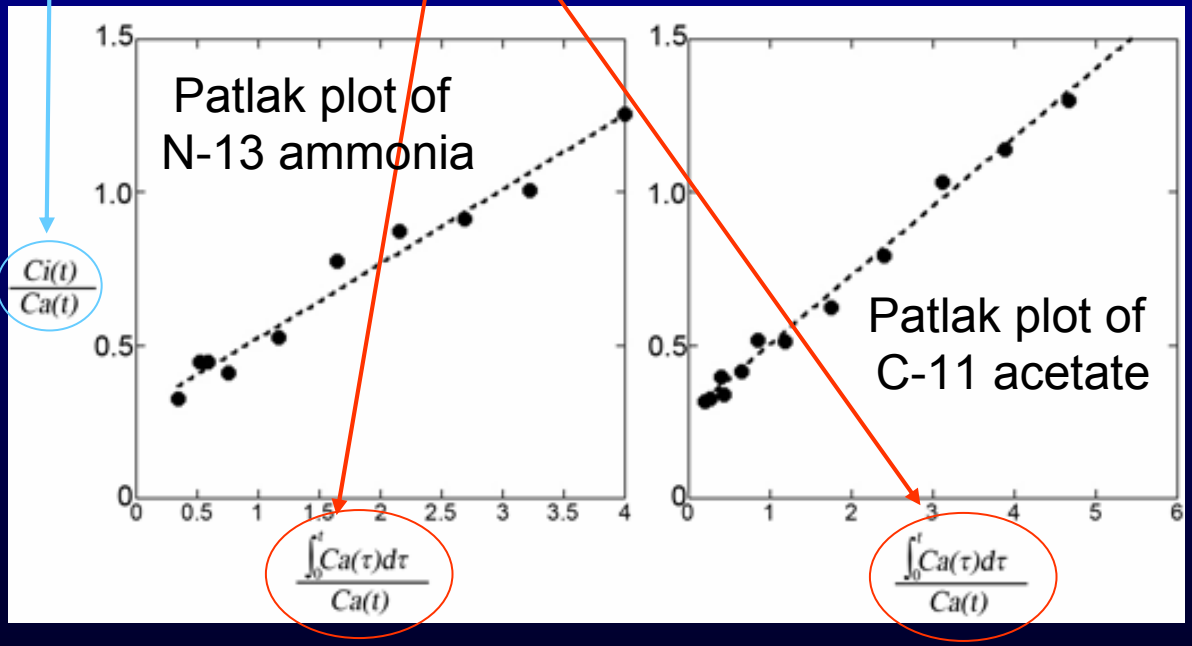
Input Phase (1~3min)
Peak (3-8min)
Washout phase(8min~

- Peak: uptake correlate with relative perfusion distribution.
  - Useful as relative perfusion image (like Tc-perfusion agent or Rb PET)
- Washout phase: Rate of washout correlate with oxidative metabolism.
  - k_{mono} as a marker for metabolism
- Input phase: Uni-directional uptake with high extraction.
  - Early phase kinetic is similar as N-13 NH_3

Absolute measurement of myocardial perfusion.

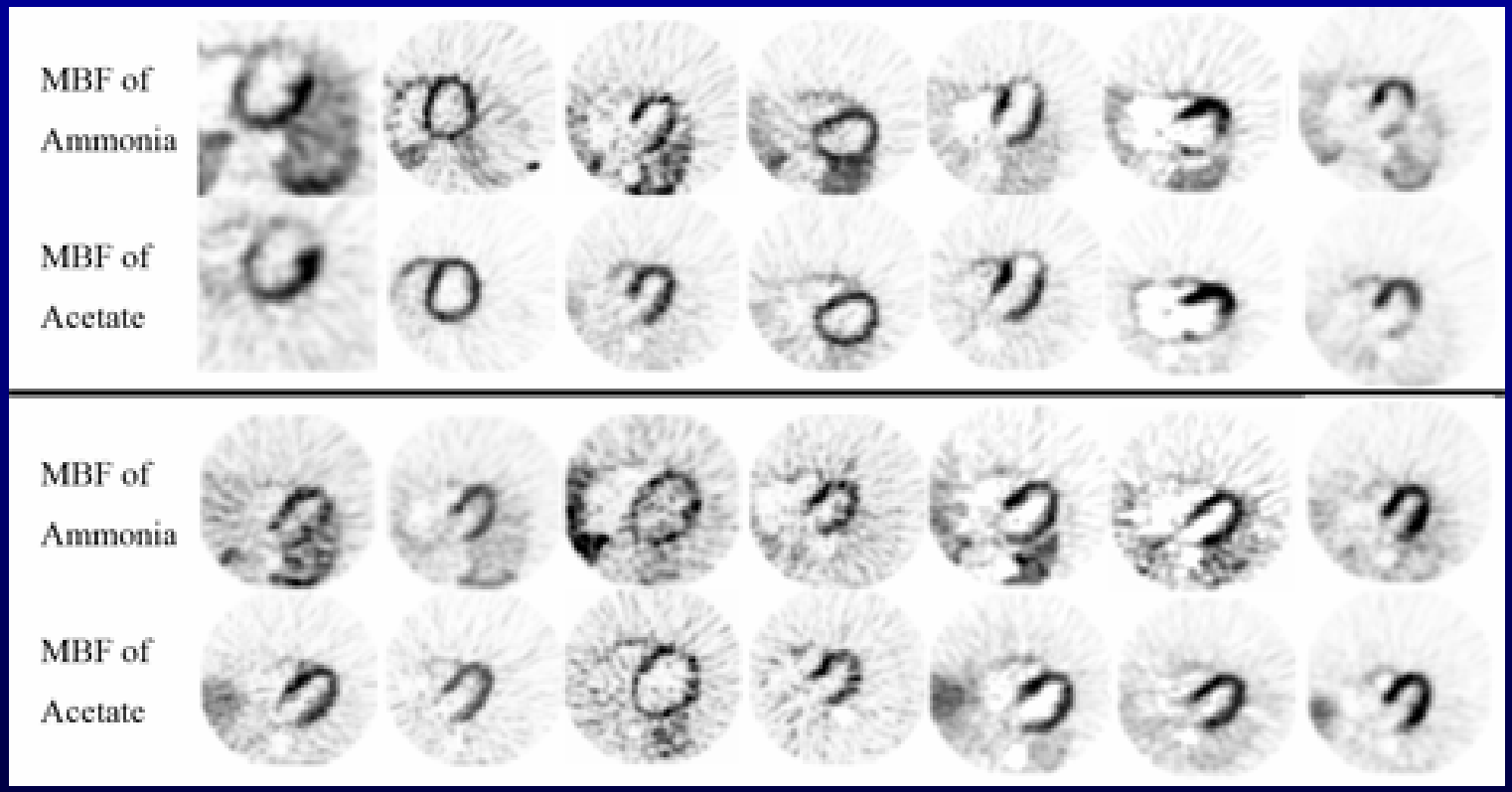
When we applied same method used in N-13 NH_3 to C-11 acetate.

$$\frac{Ci(t)}{Ca(t)} = k^* \frac{\int_0^t Ca(\tau)d\tau}{Ca(t)} + \frac{MBF^2V}{(MBF + k_3)^2} + f_b \frac{AB(t)}{Ca(t)}$$



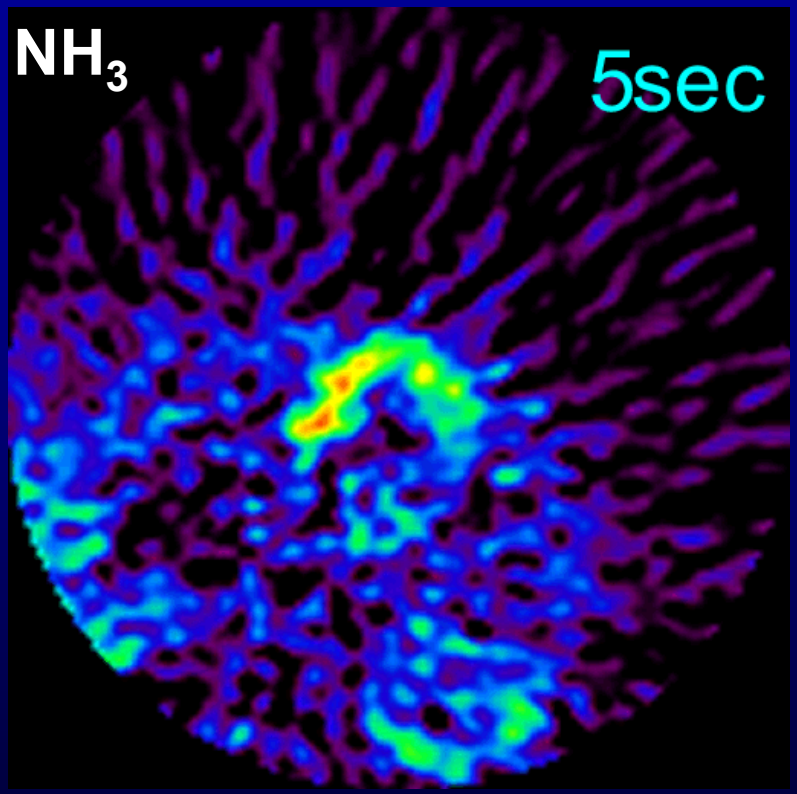
- Patlak graphical method was applied to C-11 acetate.

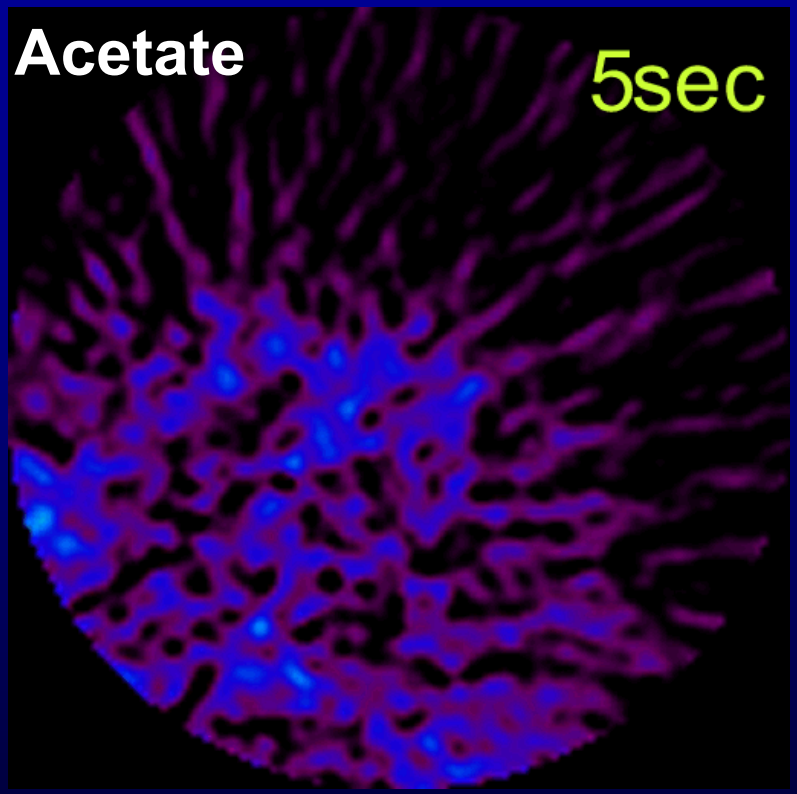
MBF image with C-11 acetate



- MBF image is created with C-11 acetate.
- Image quality is better than N-13 ammonia
- Problem; underestimation of MBF in hyperemic condition.

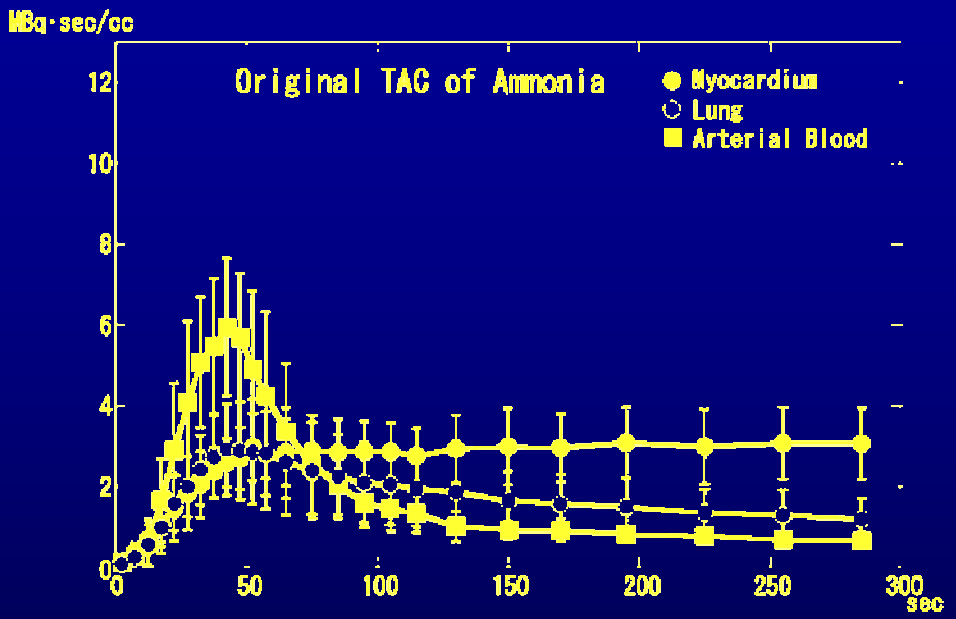
Difference of kinetic in image.

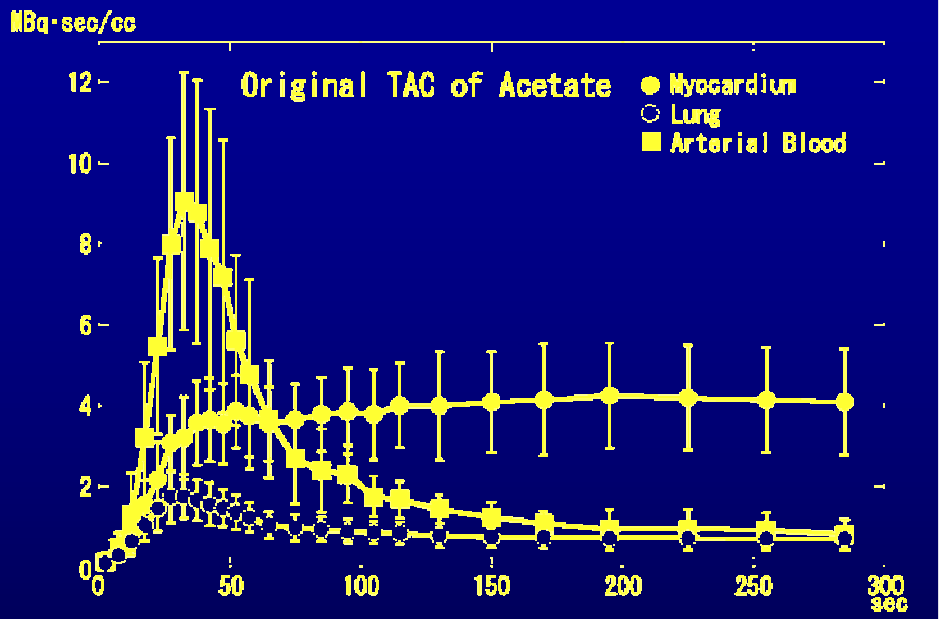




- Same radioactivity was injected. However, for N-13 NH_3, some amount of activity was trapped in the lung and does not reach myocardium.
- This difference affect the image quality of myocardium.
  - Even if the lung uptake is small, volume of lung is huge and the activity lost inlung may become also huge.

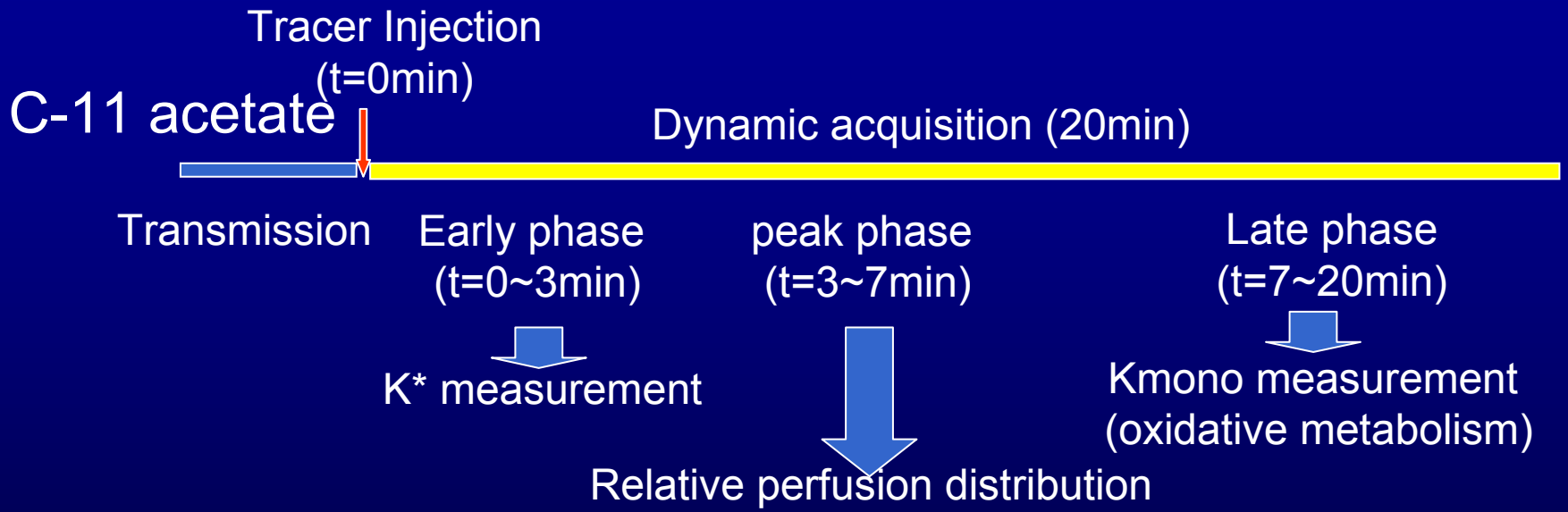
Why lung uptake of N-13 NH_3 is so high?





- Speculation;
  - Intravenously injected tracer first distributes to the lung and then reaches arterial blood and myocardium.
  - Significant amount of N-13 ammonia is trapped to the lung. This phenomenon is not apparent for the C-11 acetate.
- Question;
  - Why and how lung traps ammonia?
    - To Lung parenchyma?
    - To air space (alveolar space) as gas form?

How the C-11 Acetate images are acquired…



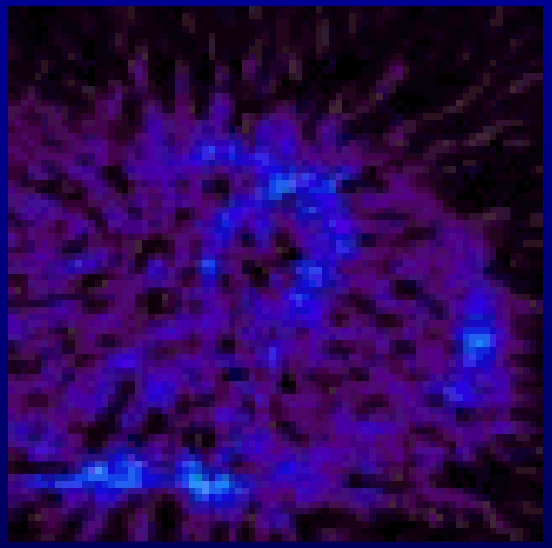
- Protocol in our institute
  - 5 sec x 12 frames
  - 10 s. x 6 fr.,
  - 20 s. x 3 fr.,
  - 30s. x 4 fr.
  - 1min x 15 fr.

The other method for MBF measurement using C-11 acetate.

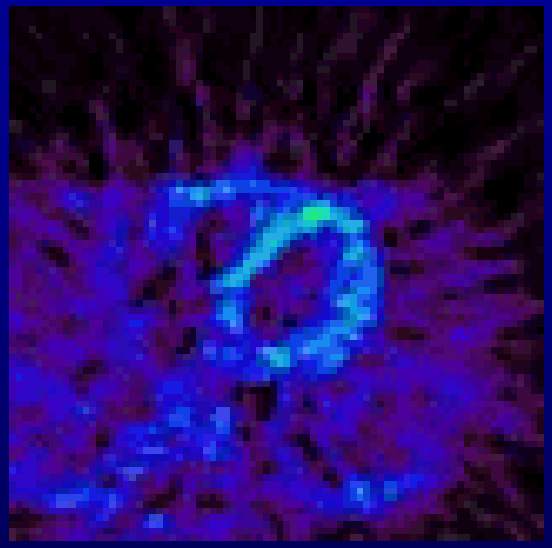
- van den Hoff J, et.al., J Nucl Med 2001; 42: p1174
  - reversible 1-tissue-compartment model.
  - Using model analysis, uptake rate constant (K_1) is calculated.
  - Formula; $K_1 = MBF*(1-0.64e^{-1.20/MBF})$
  - Use 20 min dynamic data for MBF calculation.

Several other method were reported.
There is no standardized method for MBF calculation with C-11 acetate, yet.

Things to be considered with C-11 acetate PET and k_{mono}.



k_{mono}=0.09



k_{mono}=0.06

- Normal volunteer.
  - Left; BP=124/72 HR=73 (Double product=9052)
  - Right; BP=101/62 HR=50 (Double product=5050)

k_{mono} changes according to the cardiac work.

Things to be considered with C-11 acetate PET.

- Oxidative metabolism sensitively responds to the heart rate, blood pressure, etc.
- So, oxidative metabolism is analyzed in relation with workload.
  - Kmono =0.05 with BP=200/100, HR=90

Totally different meaning

  - Kmono =0.05 with BP=100/60, HR=50

Some kind of normalization should be required.

BUT HOW?

Work Metabolic Index (WMI)

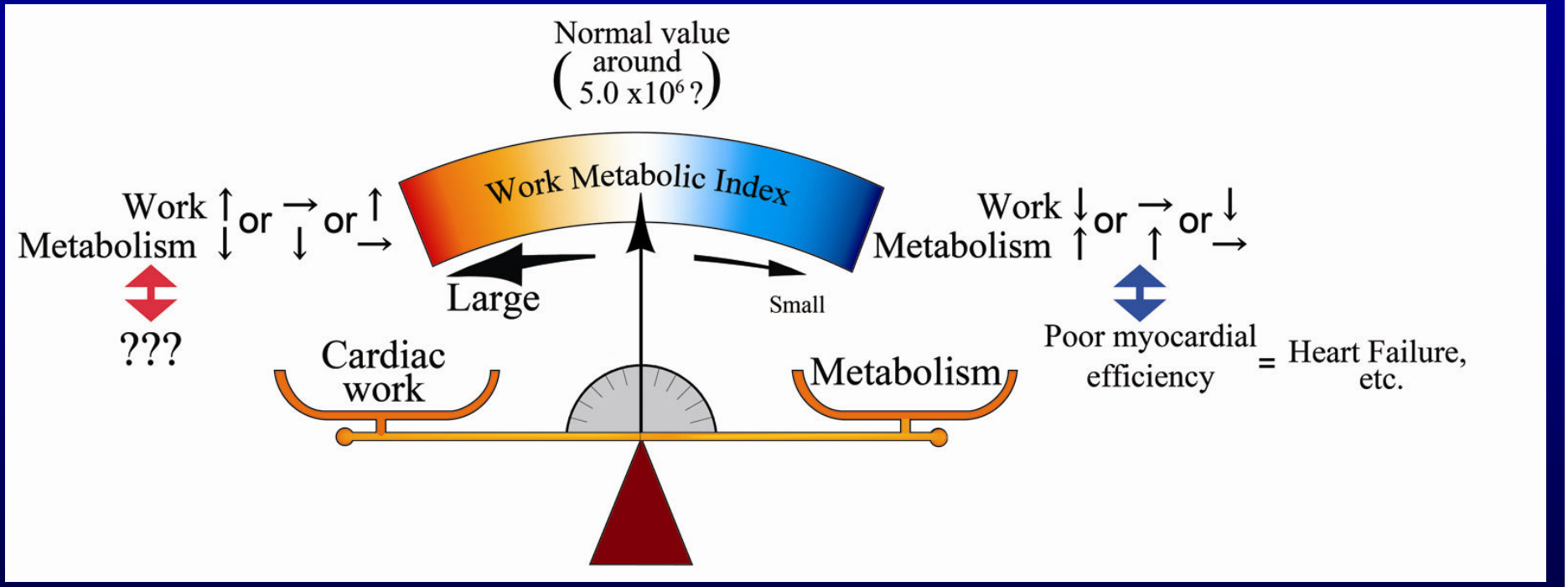
$$WMI = \frac{\text{SWI (stroke work index)} \times \text{Heart Rate}}{k_{mono}}$$

$$\textit{where} \quad SWI = \frac{\text{Systoric BP} \times \text{Stroke Volume}}{\text{Body Surface Area}}$$

$$= \frac{\text{Systoric BP} \times \text{Stroke Volume} \times \text{Heart Rate}}{k_{mono} \times \text{Body Surface Area}}$$

$$= \frac{\text{Rate Pressure Product} \times \text{Stroke Volume}}{k_{mono} \times \text{Body Surface Area}}$$

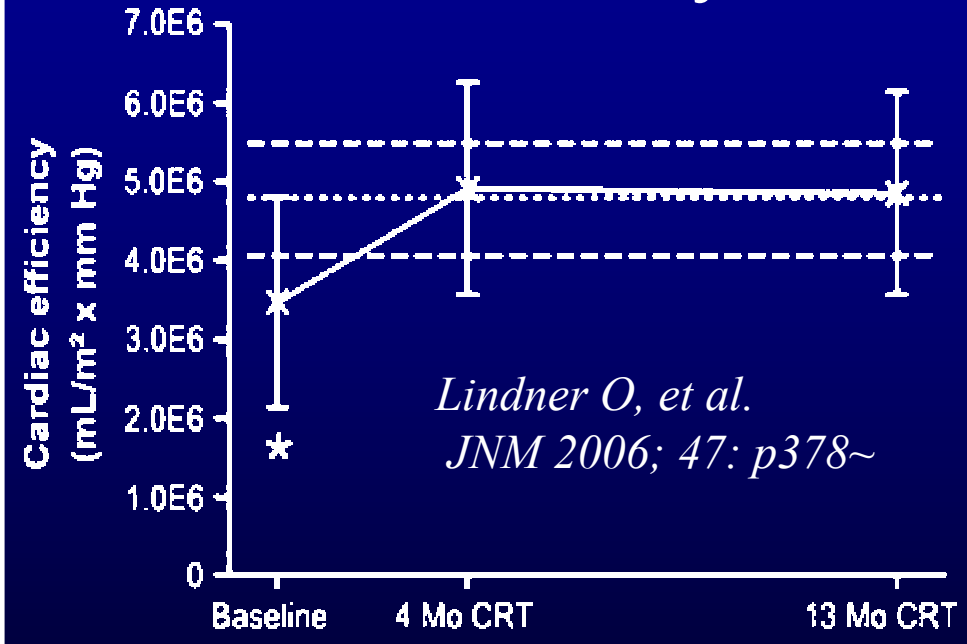
work metabolic Index (WMI)

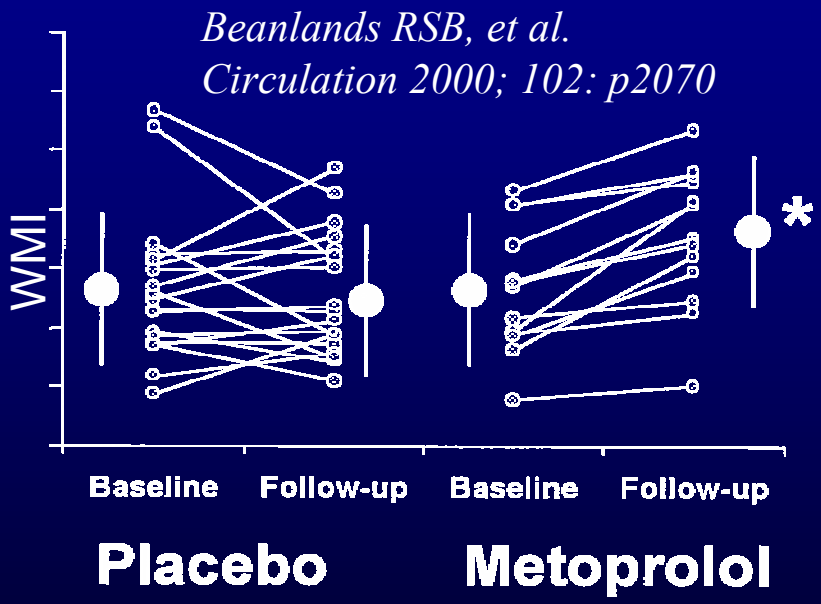


- Briefly, it is a index how the myocardium work economically. (=Myocardial Efficiency)
- Small WMI means “Bad” condition. (same work with large metabolism.)

How WMI works (how to use WMI)

- It is relatively new idea ……





Cardiac Resynchronization Therapy improves WMI in CHF

Three months treatment with β blocker improves WMI in CHF patients. It means myocardium uses oxygen more effectively.

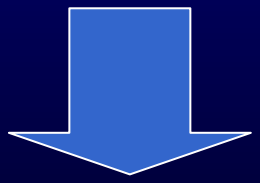
A case presentation

- 75 y.o. male
  - 2 year ago; Complete AV block was incidentally diagnosed when the patient hospitalized with pneumonia.
  - Permanent pacemaker was placed.
- This time, patient was hospitalized with heart failure.
  - No significant coronary artery stenosis.
- C-11 acetate PET study was performed.
  - k_{mono}=0.0734
    - Normal range (in our institute) ; 0.06~0.08 (Number may vary according to the double product)
  - k_{mono} / Double product =0.86x10^{-6}
    - Normal value ; around 0.7x10^{-6} ? (no matched normal database)
  - WMI=3.54 x 10^{6}
    - Normal value; around 5.0~6.0x10^{6} ? (no matched normal database)
  - EF=20%, EDV=234ml, ESV=188ml (measured by ECG gate NH3-PET)

WMI of this patient was smallest value among our record.

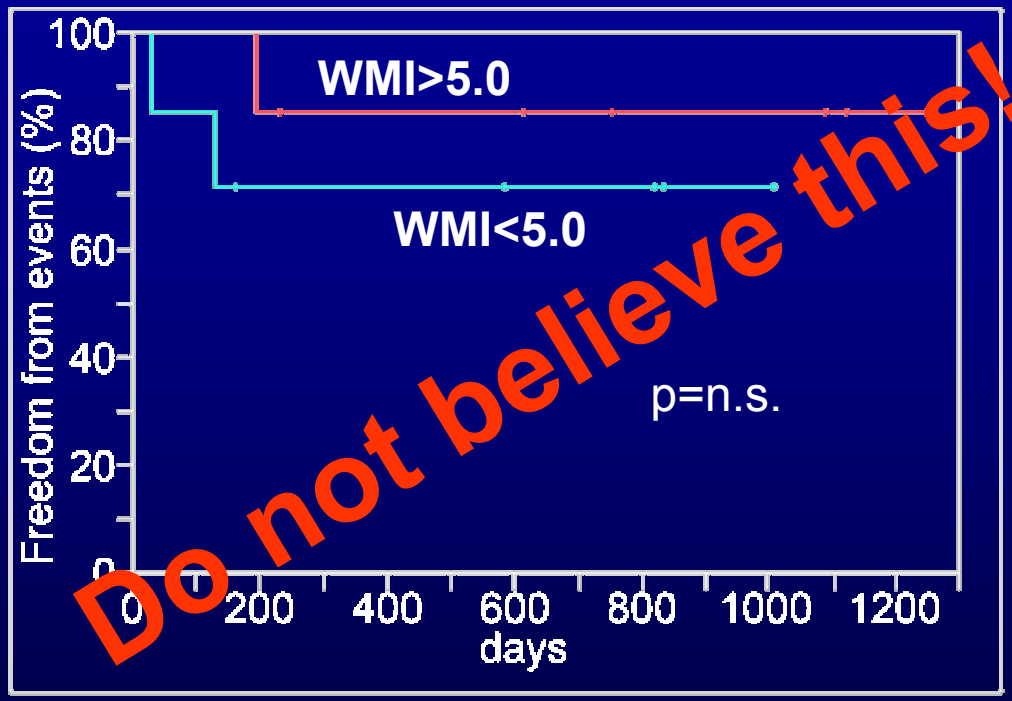
History after PET

- After patient discharged from hospital, he frequently hospitalized with heart failure symptoms.
- 4 month after PET; Hospitalized with incidental fracture.
  - Condition went wrong after this episode.
- 5 month after PET; sudden death.
  - VT?



- Relationship between WMI and prognosis in heart failure patients must be analyzed.

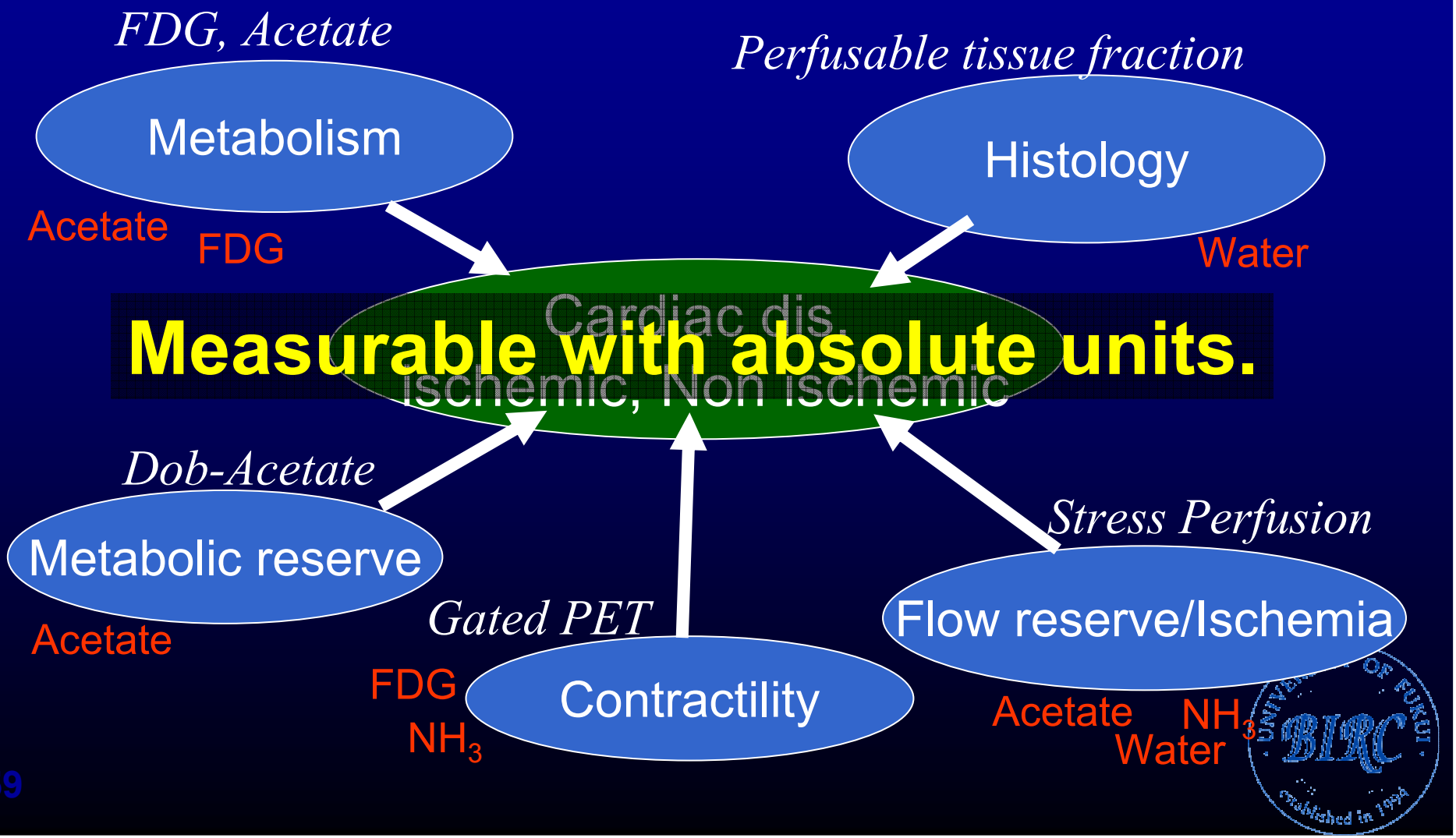
Event free survival and WMI



14 consecutive patient who underwent rest C-11 acetate PET were retrospectively analyzed.
Patients are divided into 2 groups with WMI (threshold=5.0×10^6)

- If WMI represents the relationship between myocardial energy utilization and its production, WMI may contribute to the assessment of prognosis.
- This results is very preliminary one. However, it is worthy to study the relation between WMI and prognosis.

PET is useful tool to evaluate all the aspect of cardiac disease.



Summary; Take home message

- PET can provide useful information for clinical cardiology.
  - Viability; FDG is gold standard. However, usually SPECT imaging is doing well for clinical diagnosis.
  - For future cardiology, quantitative capability of PET will provide very valuable information especially for primary and secondary preventative cardiology.
  - C-11 acetate is one of promised tracer for cardiology. It can evaluate, perfusion, and metabolism in one study. It have possibility to replace FDG and N-13 ammonia.

PET is very useful tool for cardiology.
Use PET not only for scientific study,
but also for clinical management.