

Contribution of major autohemotherapy(MAH) to antioxidant effect and endothelial cell function of artery in vivo

Ginza Oct Clinic (JAPAN)

Founder of Japanese association of ozone therapy

Kazuhiro Ito,MD.,Ph.D. A B A A M.

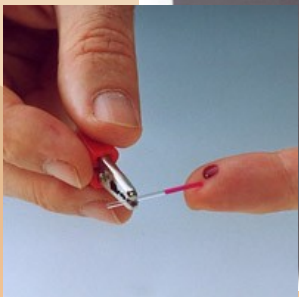
Today's menu

- ❁ Increase of Antioxidant ability after several MAH (major autohemotherapy)
- ❁ Improvement of Flow Mediated Dilatation even after one MAH
- ❁ Present situation of ozone therapy in Japan
 - MAH, Minor AH, rectal, ozone oil, ozone water

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FRAS (Free Radical Analytic System)



FRAS

- ❁ Free Radical Analytical System
- ❁ Made in Italy
- ❁ Has two features;



* **d-ROM**: test of **r**eactive **o**xygen **m**etabolites
from blood serum samples using
Fenton reaction

BAP : test of **b**iological **a**nti-oxidant **p**otential
from blood serum samples

$(\text{Fe}^{+++}) + \text{total reduced ability} \rightarrow (\text{Fe}^{++})$
=antioxidant ability

B A P

(Normal Zone = 2200 ~ 4000 μ M or μ Eq /L)

	Antioxidation potency
2200 over	Good
2200 ~ 2000	Borderline
2000 ~ 1800	A little lack
1800 ~ 1600	Lack
1600 ~ 1400	Greatly lack
Under 1400	Severely lack

BAP before & after MAH

❁ N=29

❁ Male=17 female=12

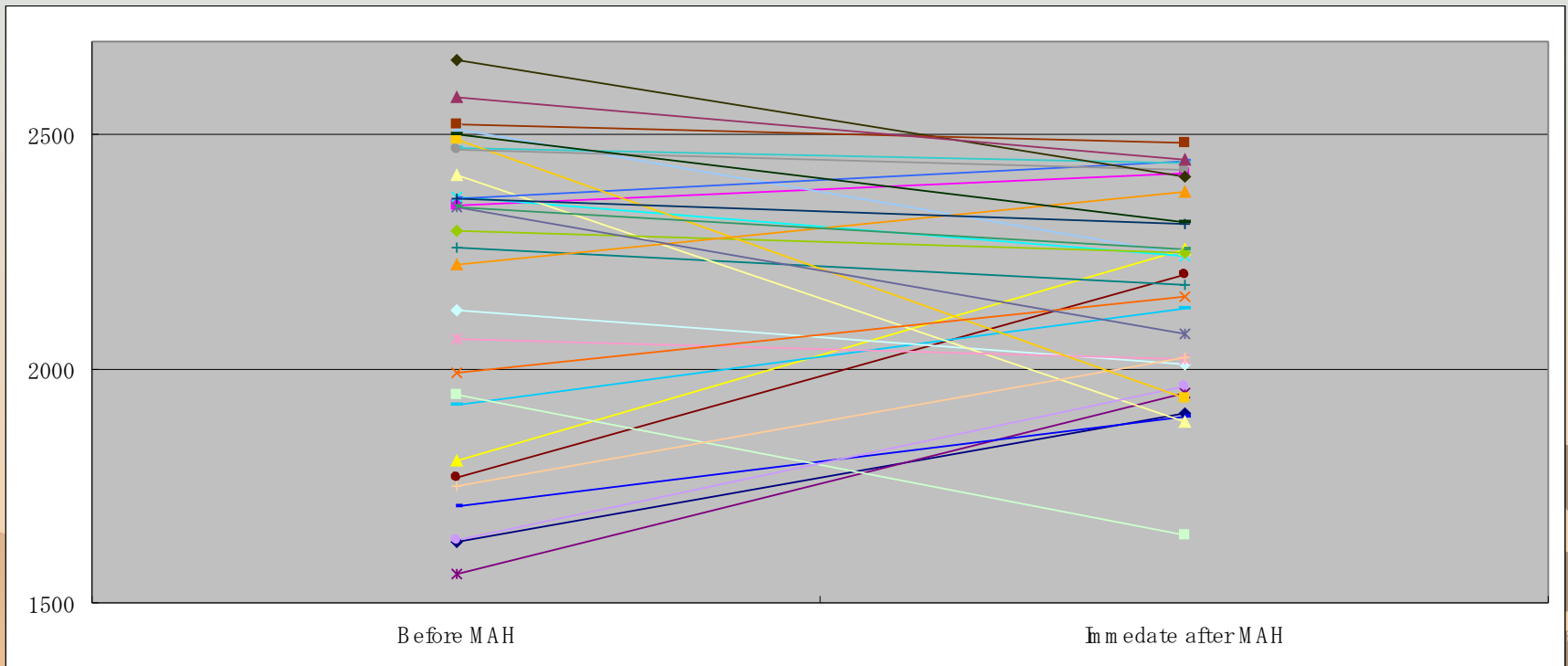
❁ Age 22~81

❁ METHOD

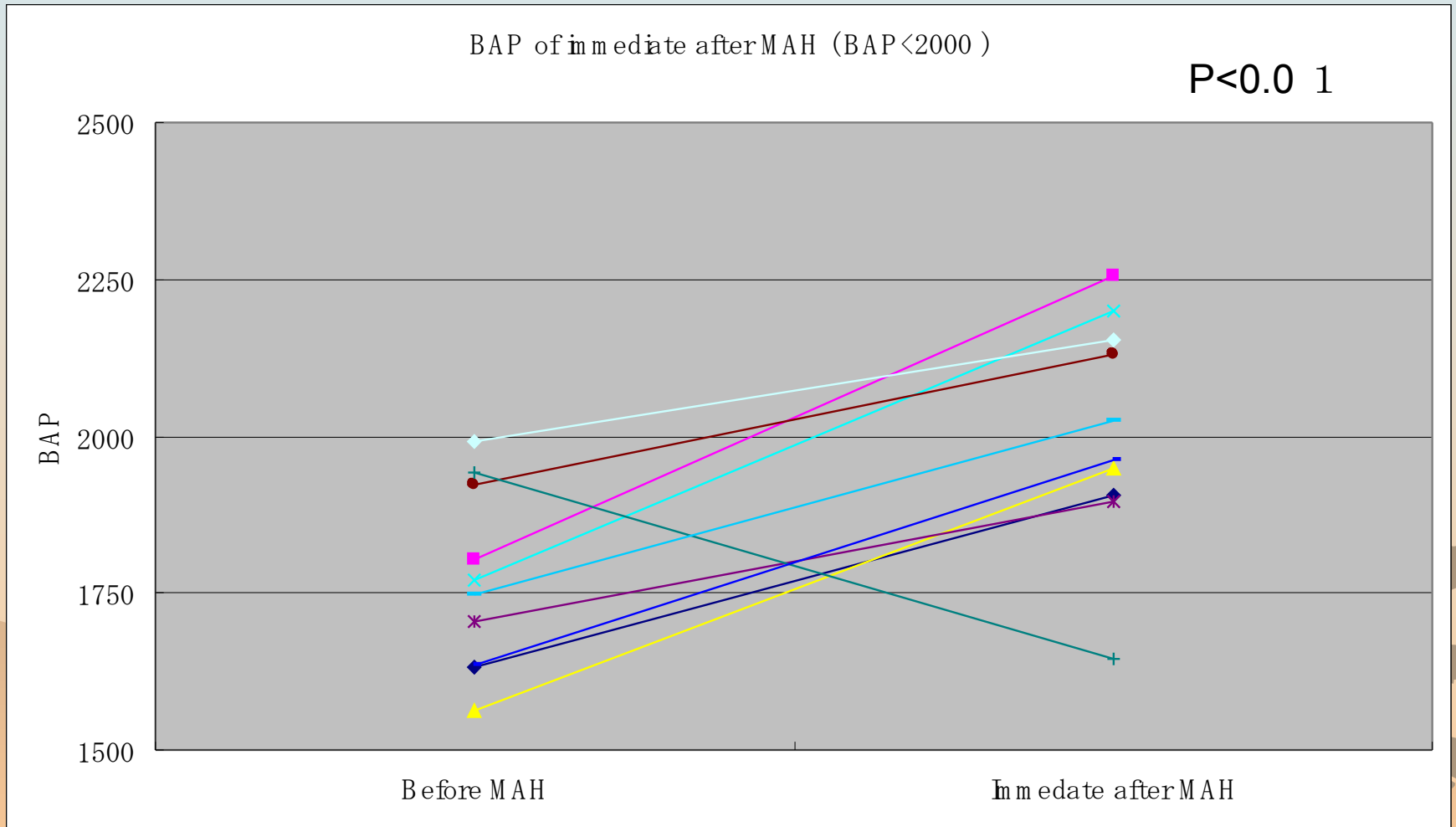
- 1. take a little blood for control of BAP
- 2. take 100ml of blood and add ozone (40 μ g 100ml)
- 3. take a little blood for BAP when transfusion finished

BAP before & after MAH

No significant differences



BAP before & after MAH (BAP < 2000)



BAP

test of biological anti-oxidant potential from blood serum samples

❁ N=25

❁ Male=10 female=15

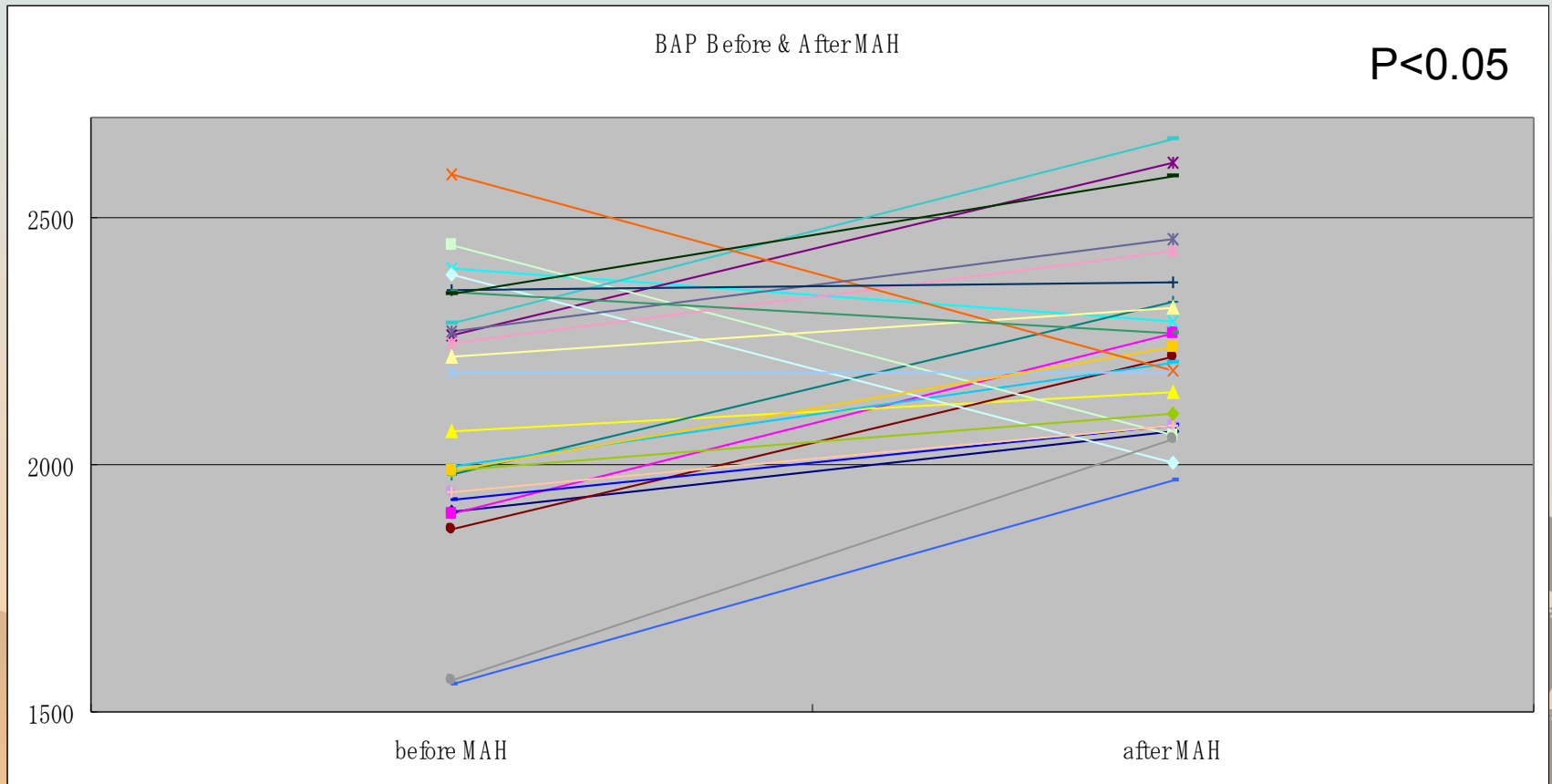
❁ Age 35~77

❁ METHOD

- 1. take some blood on first visit to my clinic before any treatments
- 2. after several MAH, take a little blood for BAP test, this is taken just before that day's MAH treatment

BAP

test of biological anti-oxidant potential from blood serum samples



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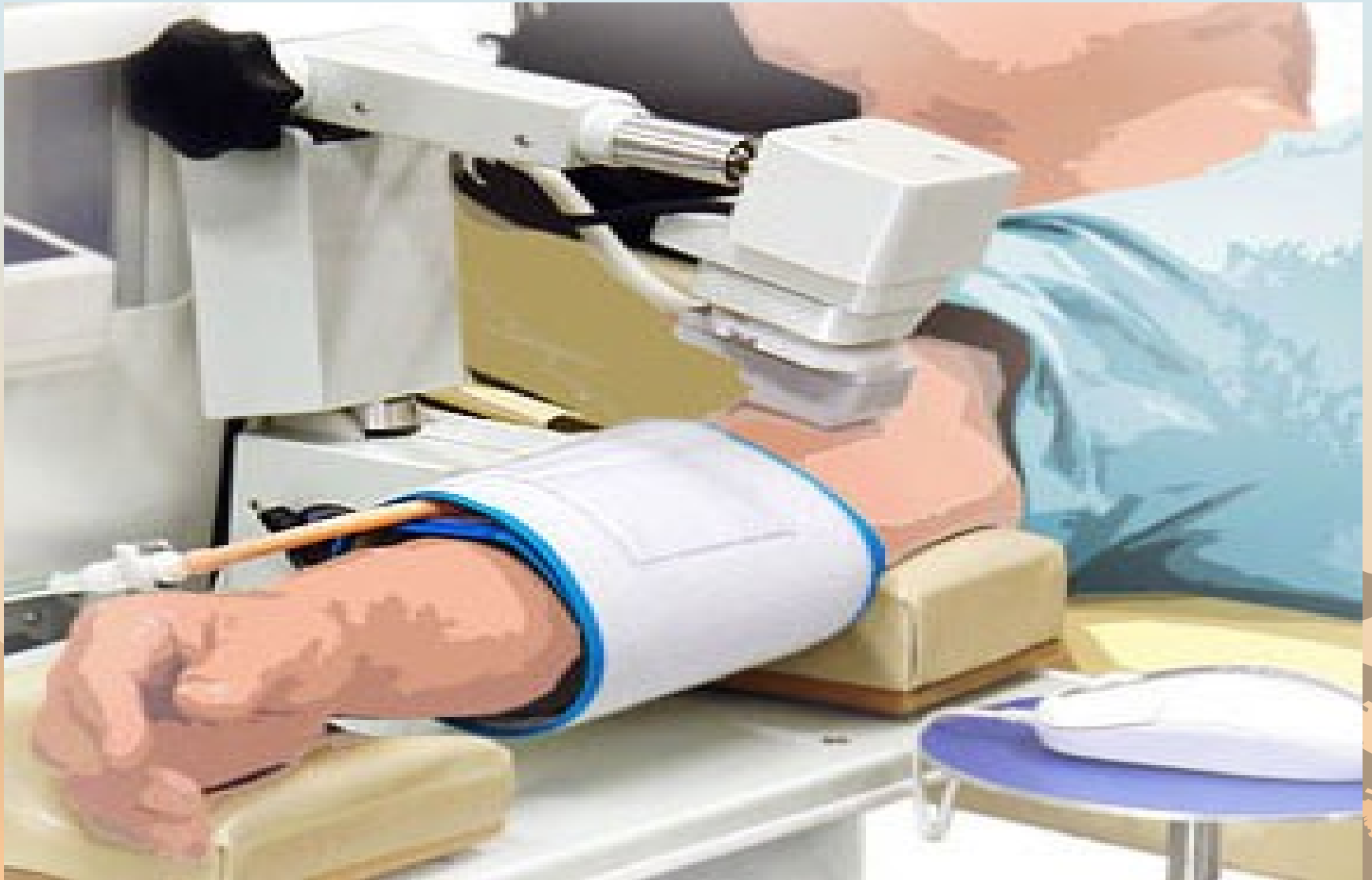
FMD

- ❁ Flow-Mediated dilation (FMD)
- ❁ Reflects endothelium-dependent vasodilator **function**, not analyzing the lumen diameter
- ❁ Dependent on endothelium-derived NO
(EDNO)
- ❁ Non-invasive

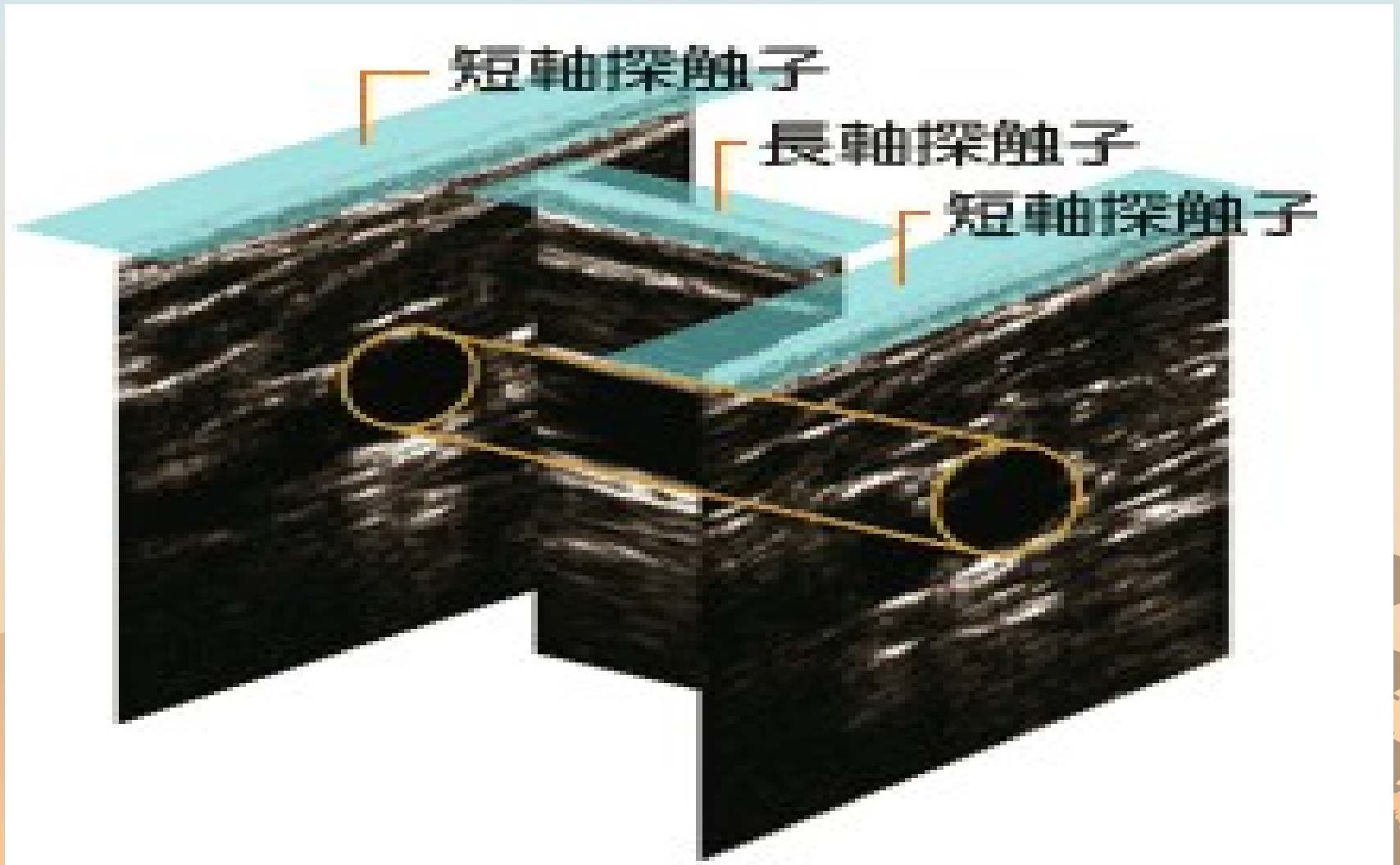
UNEX-EF



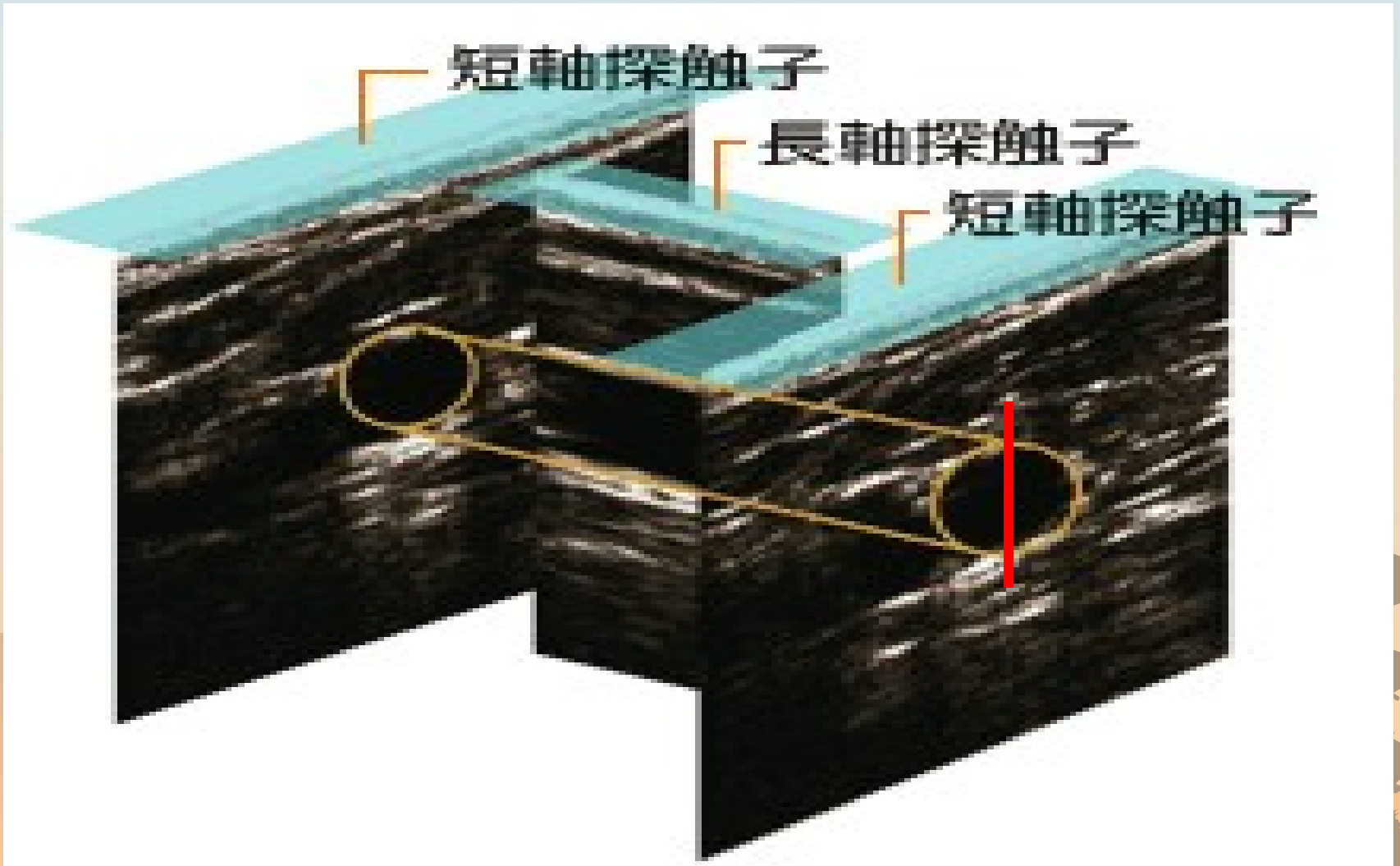
UNEX-EF



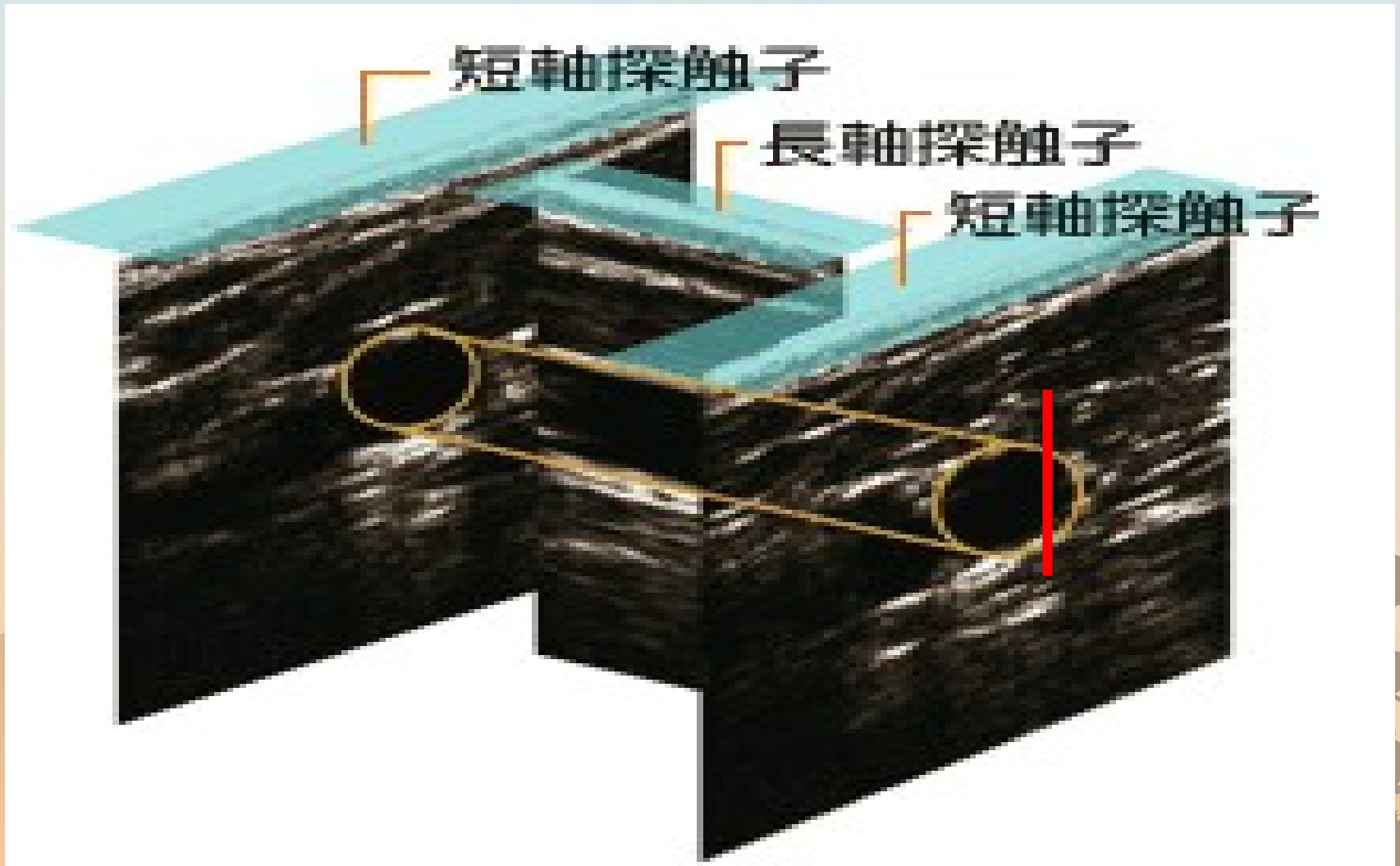
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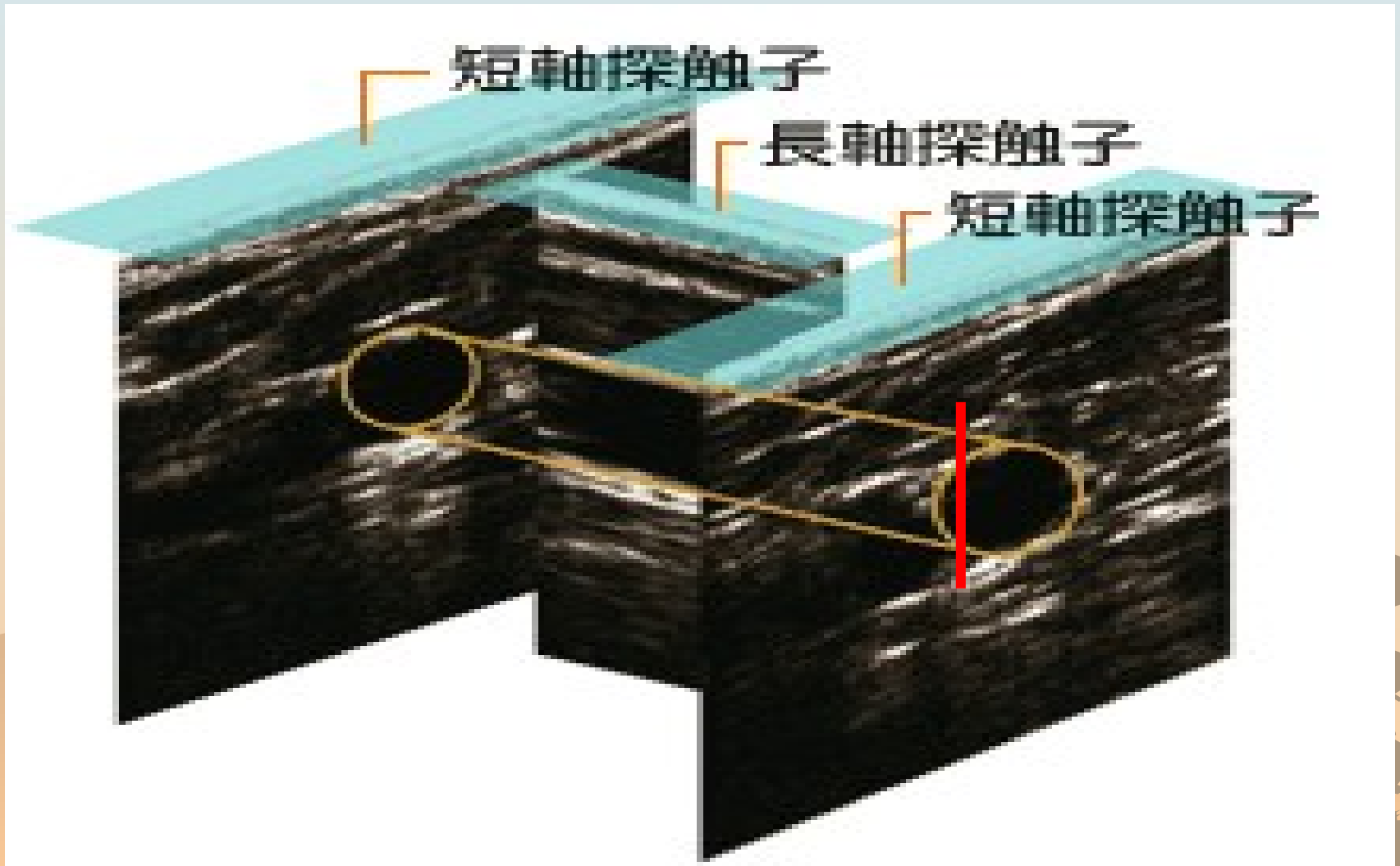
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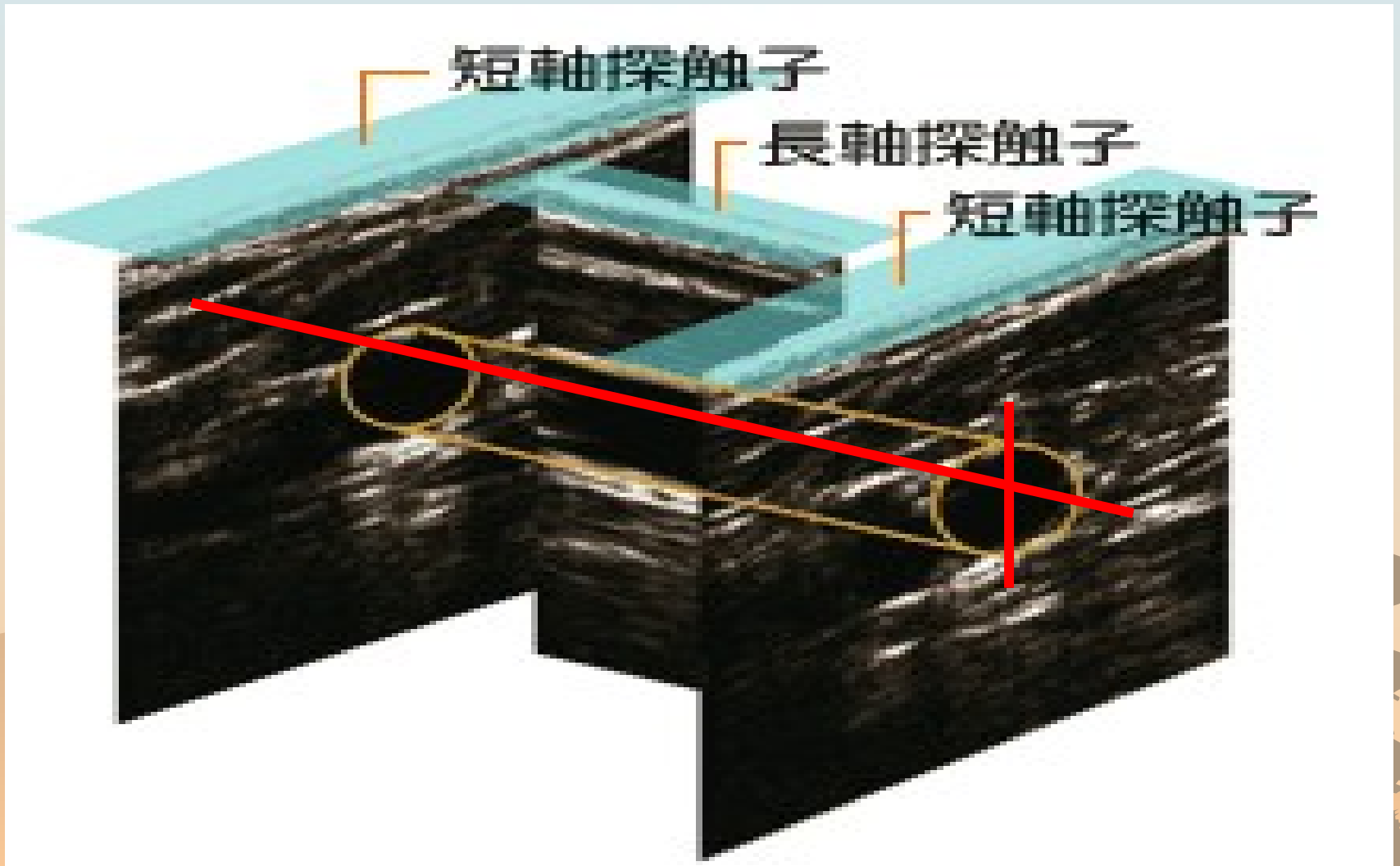
Former machines



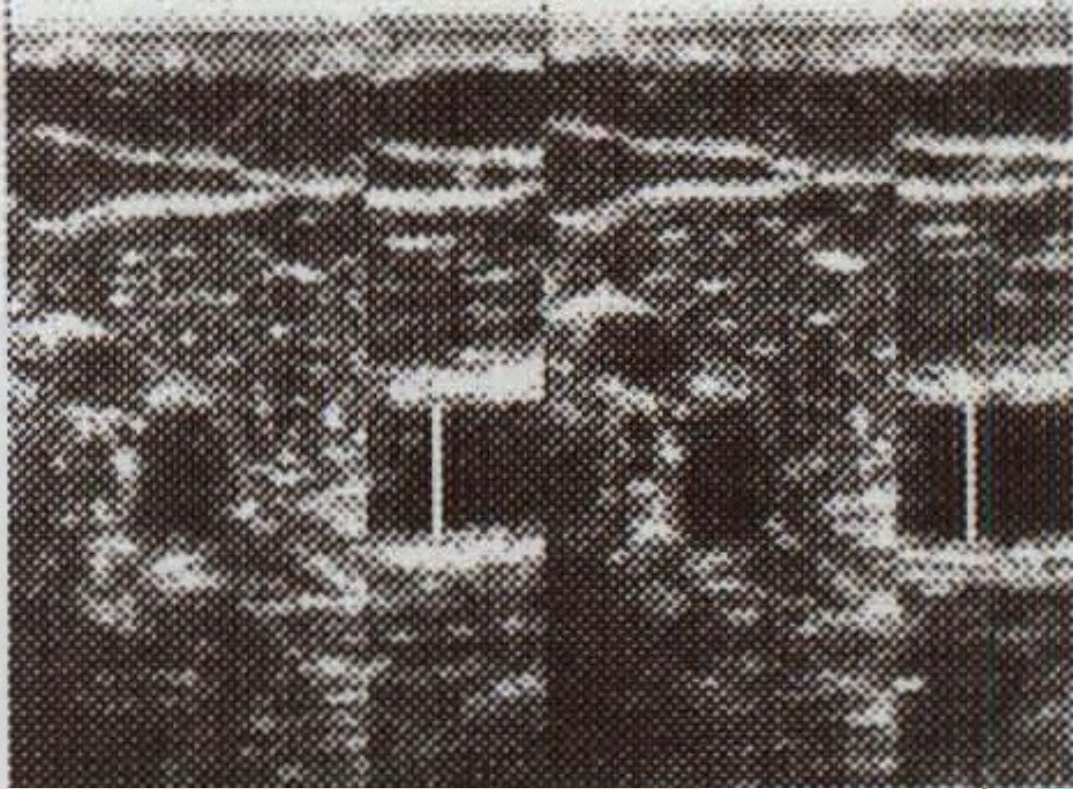
Former machines



UNEX-EF



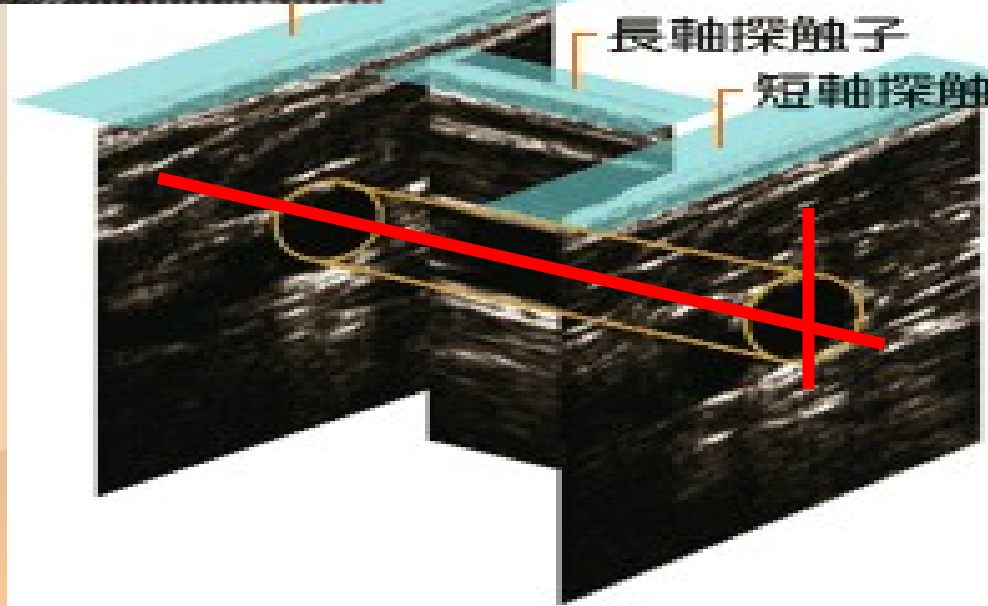
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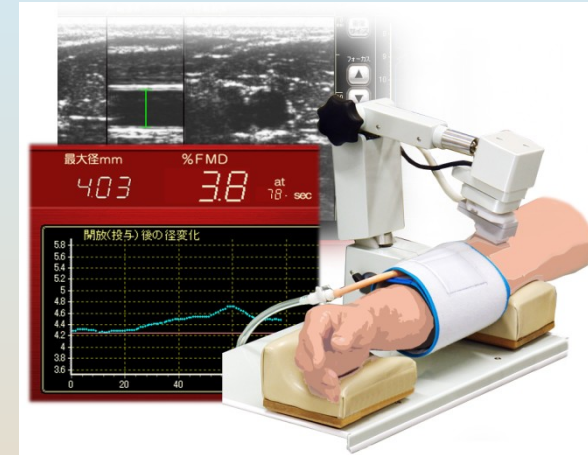
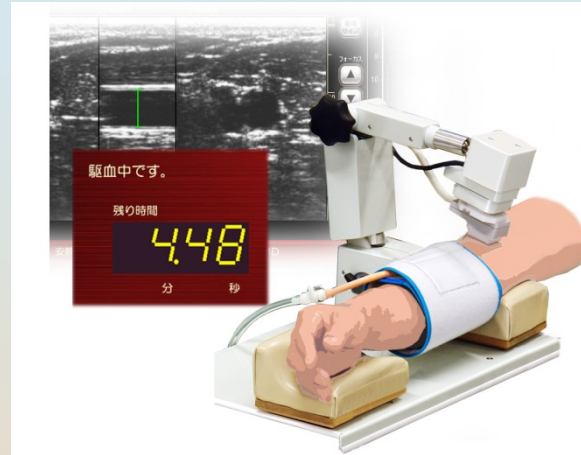
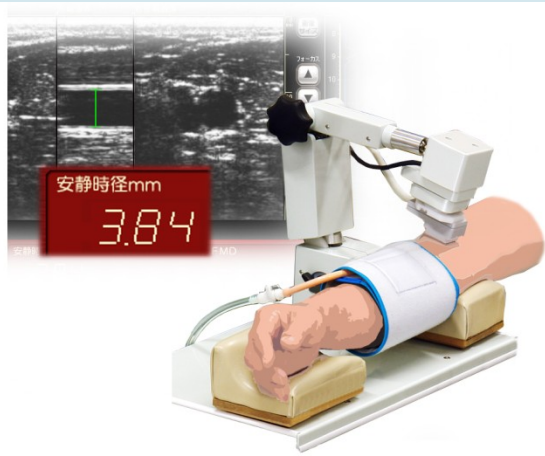
短軸探触子

長軸探触子

短軸探触子



FMD

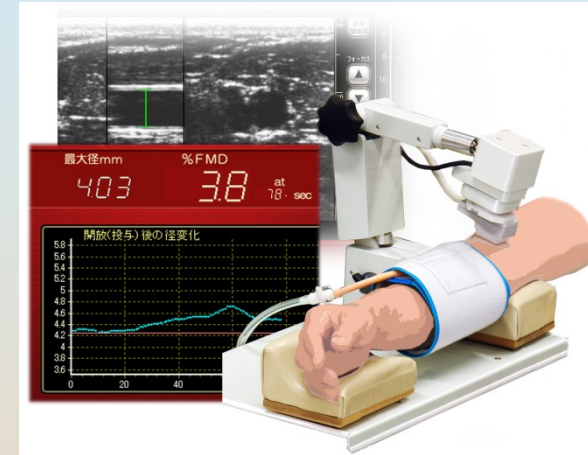
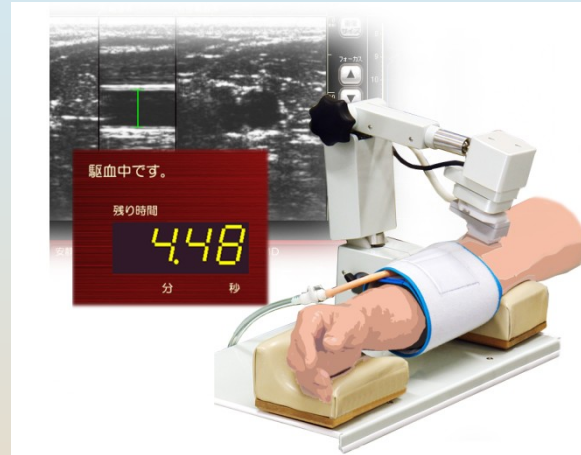
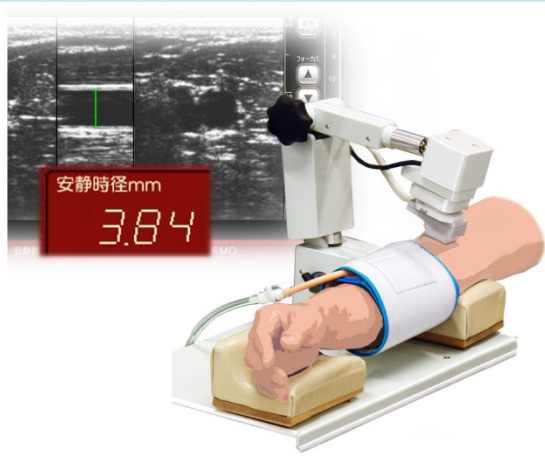


1. Resting
measure the diameter of
brachial artery

2. Tourniquet for 5 min
stop blood flow at
systolic pressure + 50mmHg

3. Measure the diameter of
brachial artery after release
the tourniquet.

FMD



1. Resting
measure the diameter of
brachial artery

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stop blood flow at
systolic pressure + 50mmHg

3. Measure the diameter of
brachial artery after release
the tourniquet.

FMD (%)

$$\text{FMD (\%)} = \frac{\text{max diameter} - \text{resting diameter}}{\text{Resting diameter}} \times 100$$

FMD

5% < border < 8%
subnormal normal



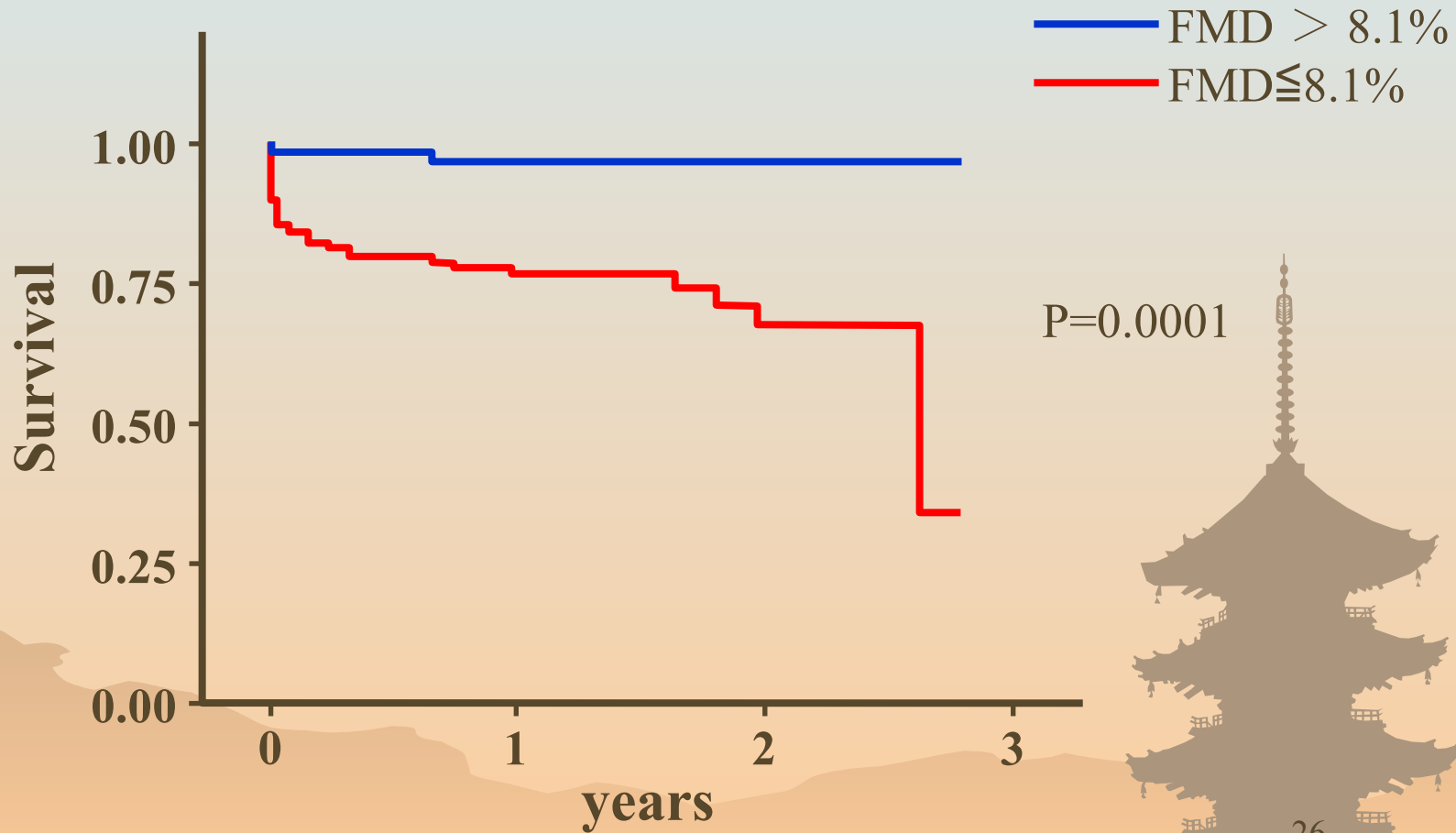
FMD

- ❁ Good FMD → Good prognosis of CVD
- ❁ Poor FMD → Poor prognosis of CVD



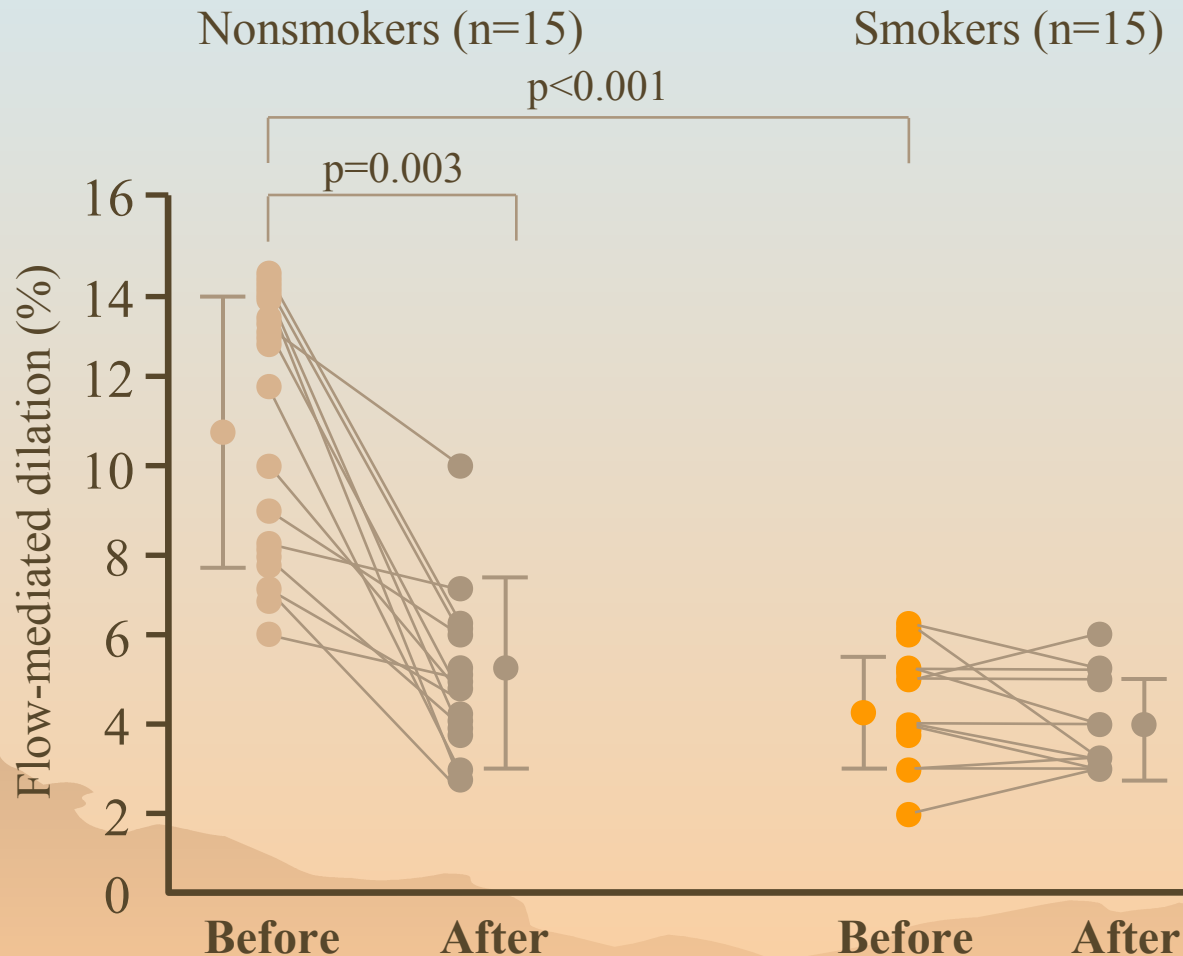
FMD and Prognosis

peripheral artery occlusion patients n=199



Passive smoking and FMD

FMD of non-smokers decreased the same as that of smokers in 30 min

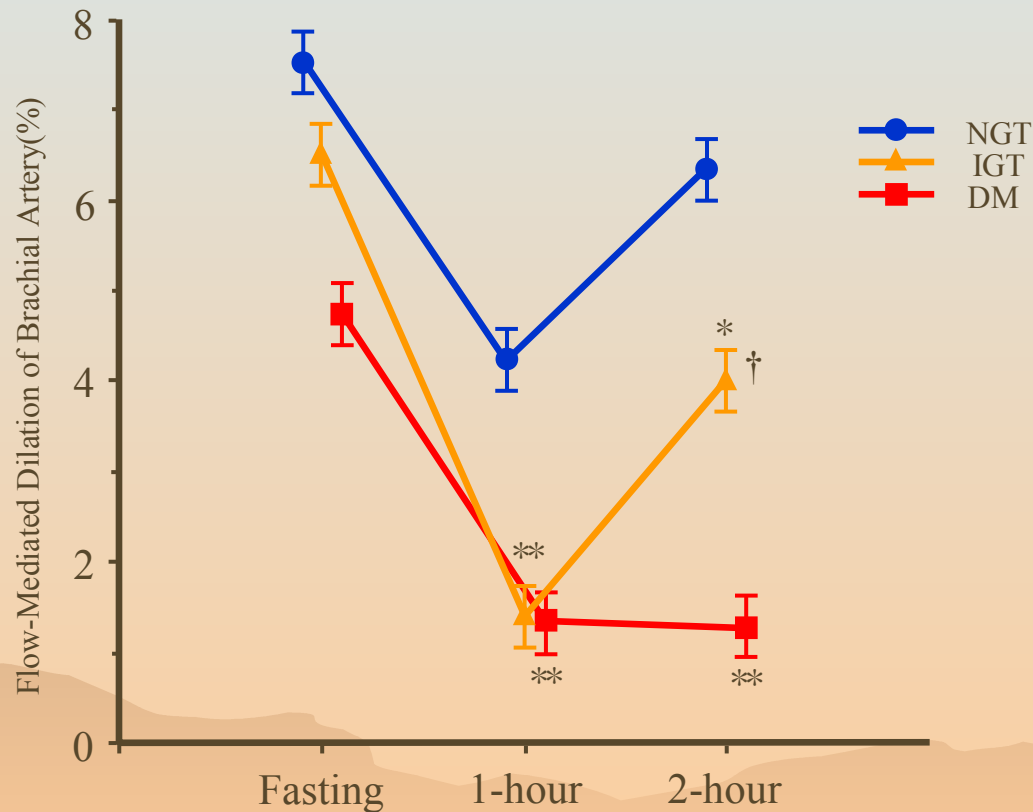


Blood sugar level of OGTT and FMD

58 subjects

(17 patients with NGT, 24 with IGT, and 17 with type 2 DM)

*p<0.01, versus fasting; **p<0.005, versus fasting ; †p<0.01, versus 1 h.



Change of FMD after MAH

❁ N=6

❁ Male=2 female=4

❁ Age 22~71

❁ METHOD

- 1.measure FMD at resting position
- 2. Tourniquet for 5 min
- 3. measure FMD immediately after release the tourniquet

Before MAH 22Y Female

FMD検査結果

検査日 2008/11/21 17:40:39 検者

被検者ID : 06
 氏名 :
 生年月日 :
 性別 :
 メモ :

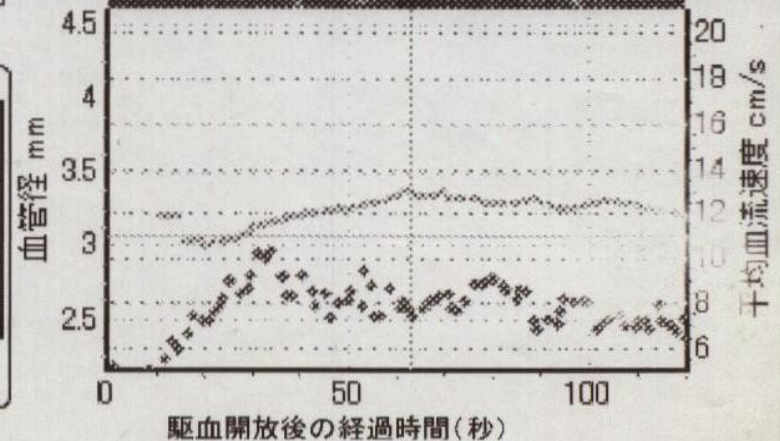
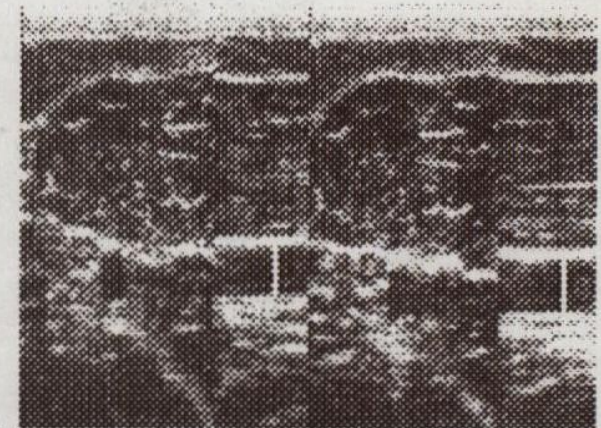
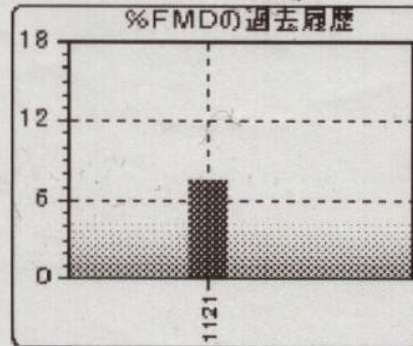
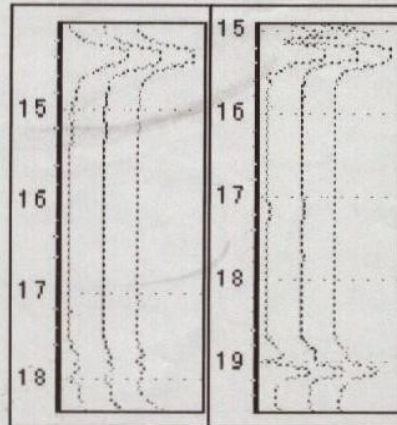
解析結果

FMD値 **7.5 %**

計測値

安静時血管径 3.07 mm
 最大拡張血管径 3.30 mm
 拡張量 0.23 mm
 at 63 s
 血流増大率 1.4 倍
 at 34 s
 (駆血部位: 計測腕:)
 平均心拍数 84 bpm
 血压 最高 0 mmHg
 最低 0 mmHg

安静時 最大拡張時



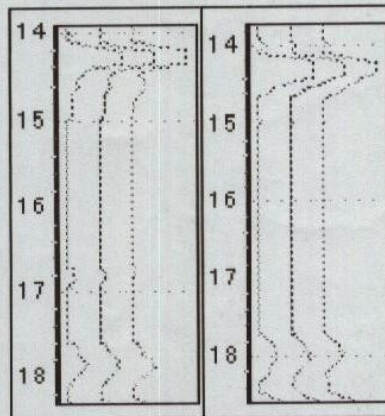
After MAH 22Y Female

FMD検査結果

検査日 2008/11/21 18:16:17 検者

被検者ID : 06
 氏名 :
 生年月日 :
 性別 :
 メモ :

安静時 最大拡張時

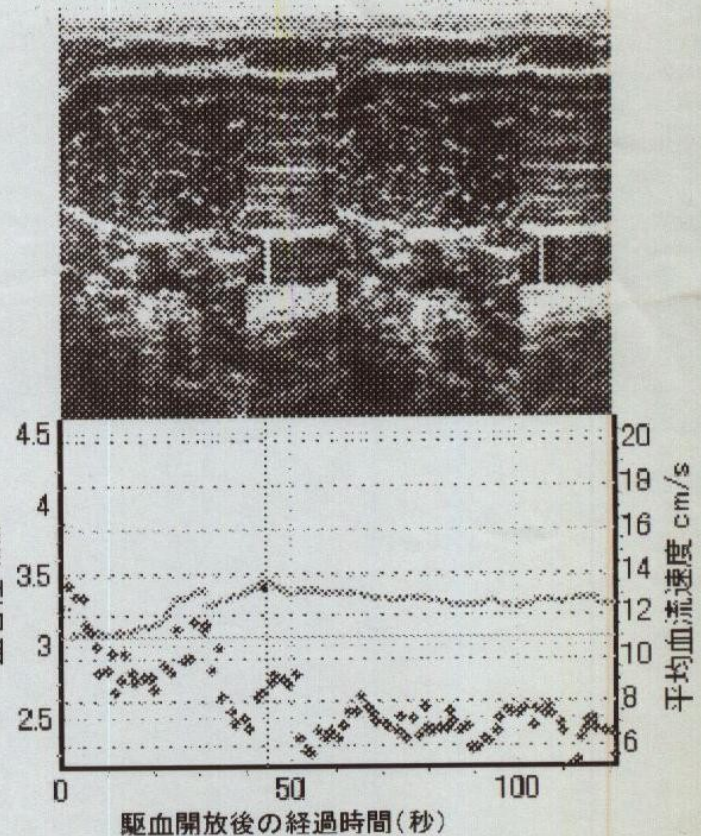
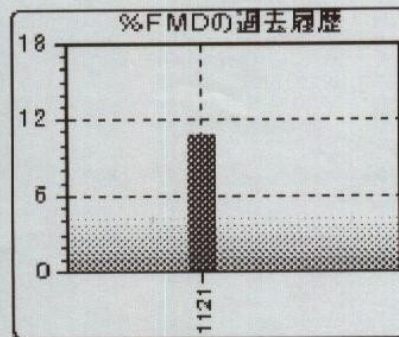


解析結果

FMD値 10.7 %

計測値

安静時血管径	3.07 mm
最大拡張血管径	3.40 mm
拡張量	0.33 mm
at	45 s
血流増大率	1.9 倍
at	1 s
(駆血部位: 計測腕:)	
平均心拍数	88 bpm
血压 最高	0 mmHg
最低	0 mmHg



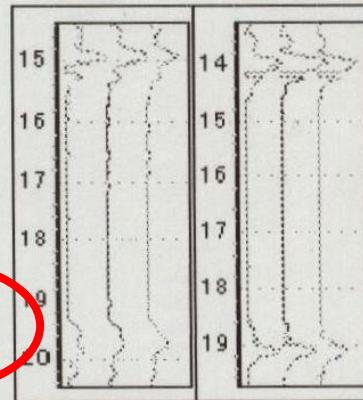
Before MAH 28Y Female

FMD検査結果

検査日 2008/11/21 11:21:55 検者

被検者ID: 1
 氏名 :
 生年月日 :
 性別 : 女性
 メモ :

安静時 最大拡張時



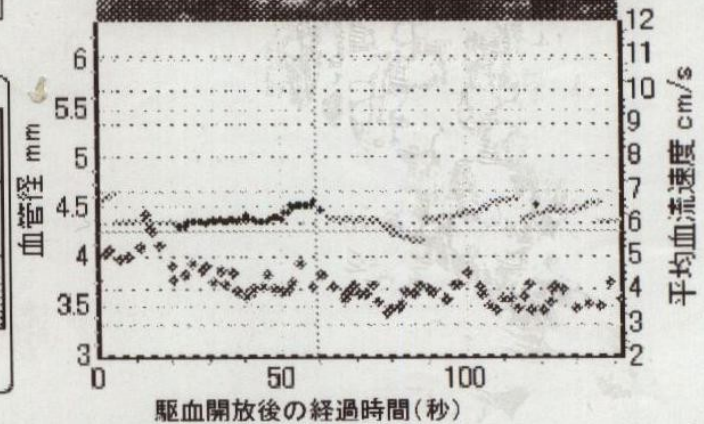
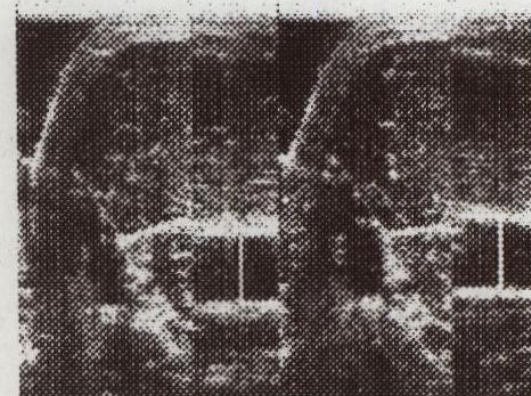
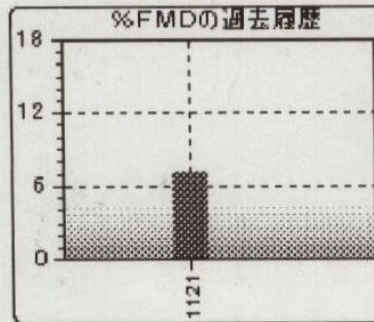
解析結果

FMD値

7%

計測値

安静時血管径 4.26 mm
 最大拡張血管径 4.56 mm
 拡張量 0.30 mm
 at 60 s
 血流増大率 1.5 倍
 at 13 s
 (駆血部位: 計測腕:)
 平均心拍数 71 bpm
 血压 最高 0 mmHg
 最低 0 mmHg



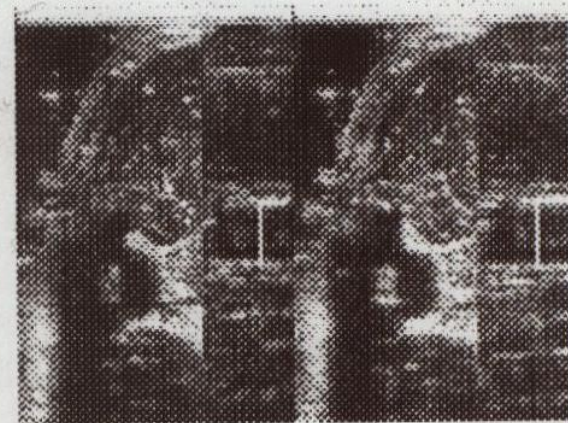
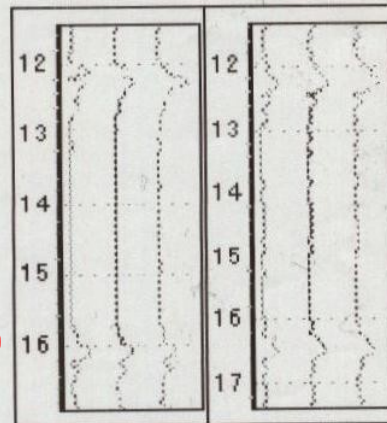
After MAH 28Y Female

FMD検査結果

検査日 2008/11/21 12:25:12 検者

被検者ID : 1
 氏名 :
 生年月日 :
 性別 :
 メモ :

安静時 最大拡張時

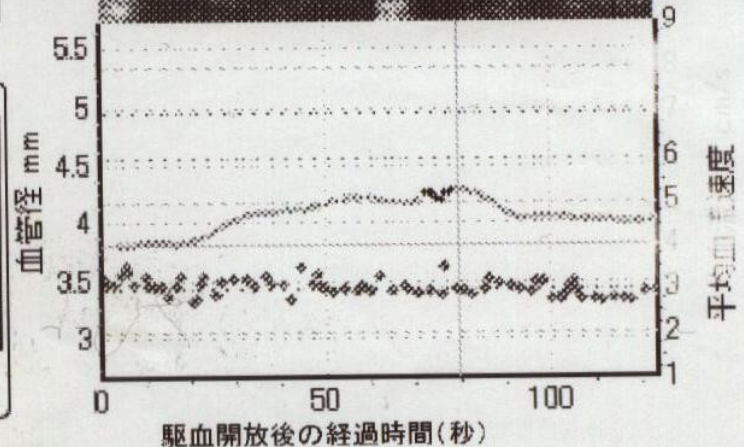
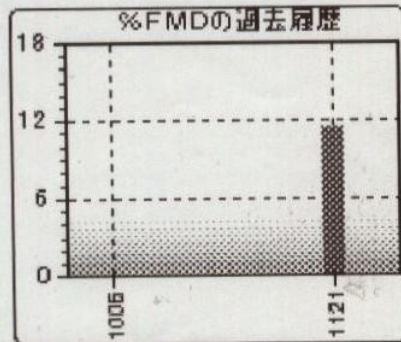


解析結果

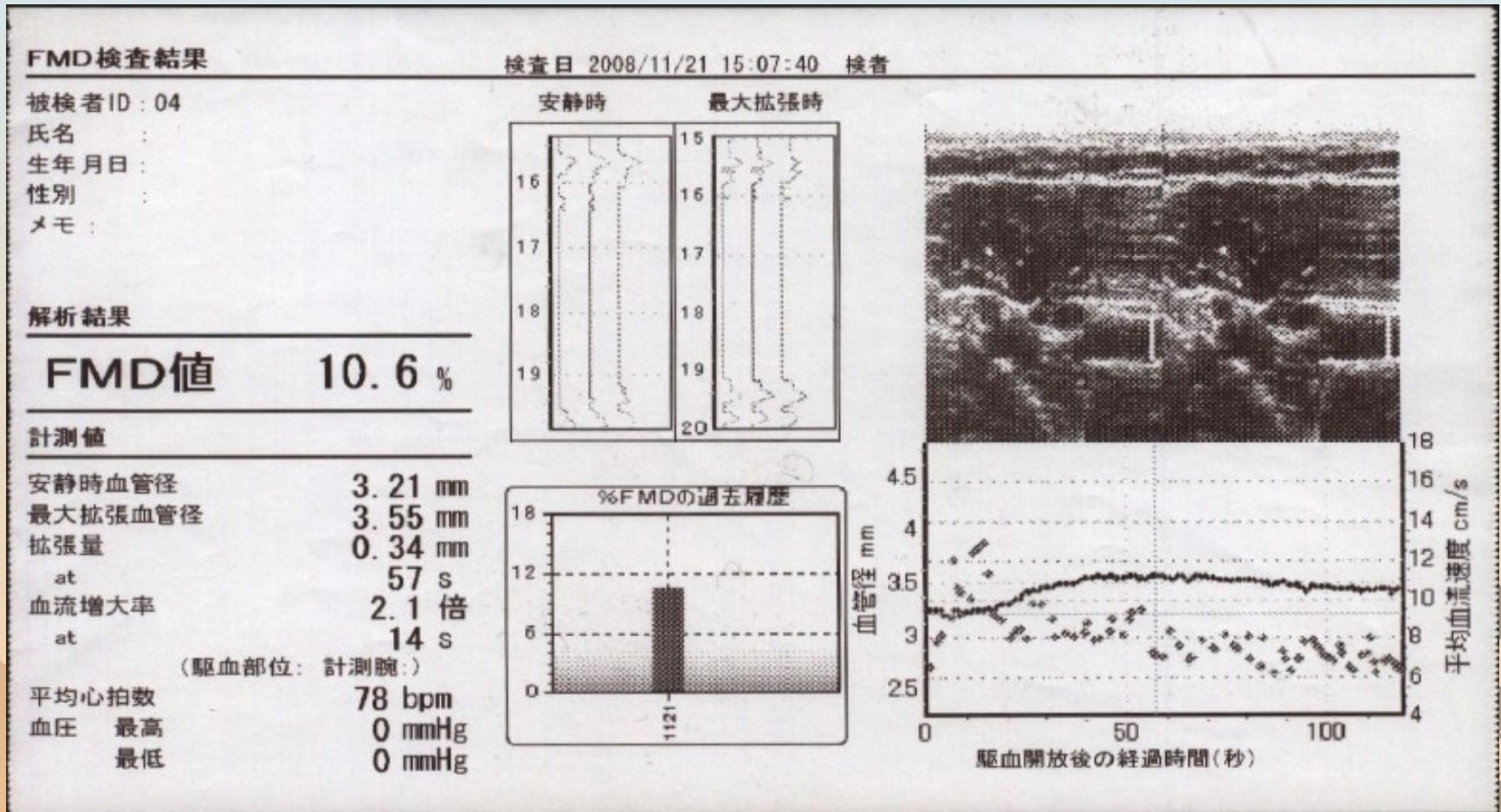
FMD値 11.5 %

計測値

安静時血管径	3.81 mm
最大拡張血管径	4.25 mm
拡張量	0.44 mm
at	79 s
血流増大率	1.2 倍
at	44 s
(駆血部位: 計測腕:)	
平均心拍数	65 bpm
血压 最高	0 mmHg
最低	0 mmHg



Before MAH 27Y Female



After MAH 27Y Female

FMD検査結果

検査日 2008/11/21 16:01:59 検査者

被検者ID: 04

氏名 :
生年月日 :
性別 :
メモ :

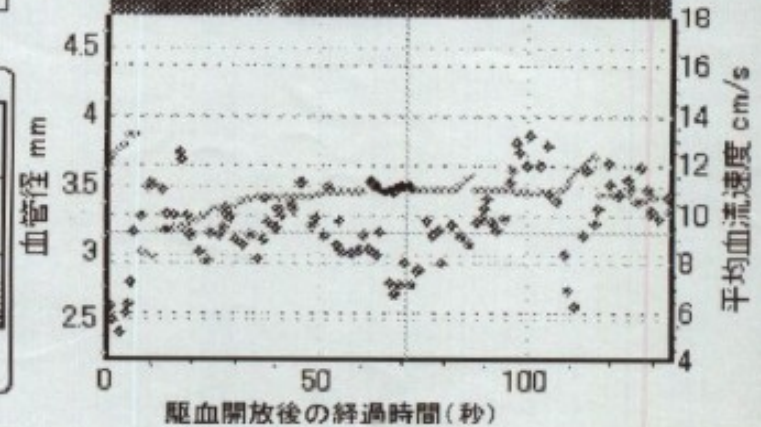
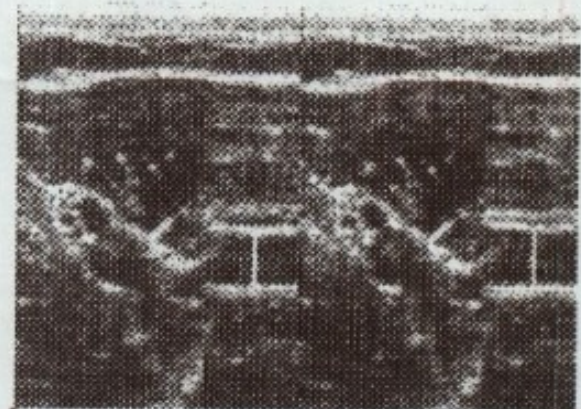
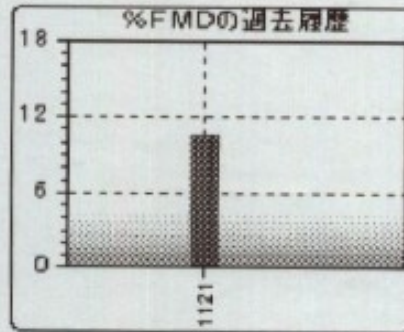
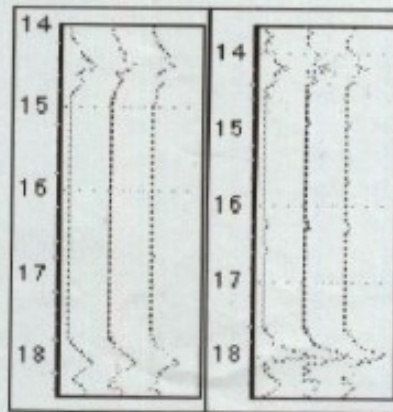
解析結果

FMD値 10.2 %

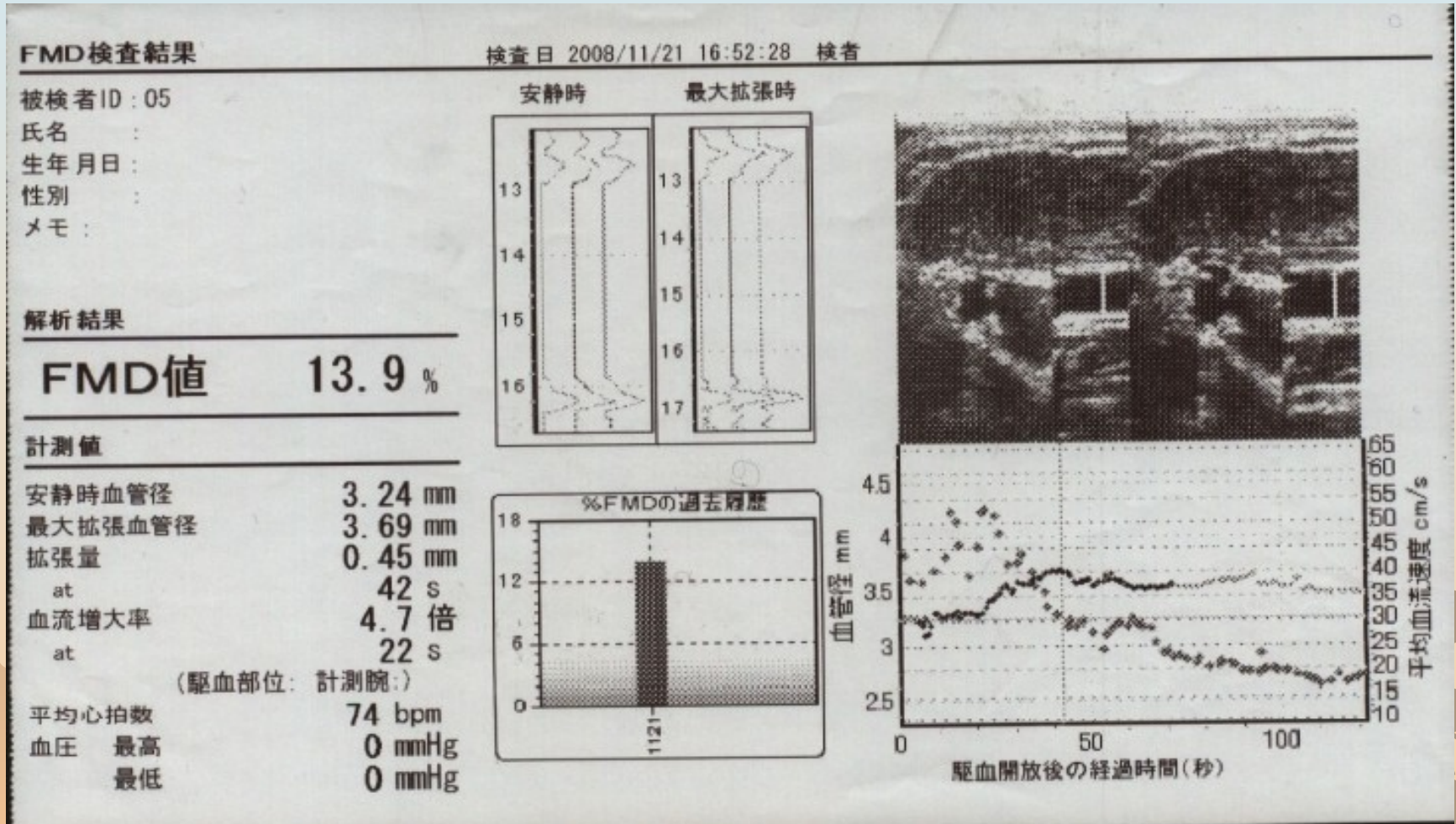
計測値

安静時血管径	3.15 mm
最大拡張血管径	3.47 mm
拡張量	0.32 mm
at	72 s
血流増大率	2.1 倍
at	16 s
(駆血部位: 計測腕:)	
平均心拍数	86 bpm
血压 最高	0 mmHg
最低	0 mmHg

安静時 最大拡張時



Before MAH 25Y Female



After MAH 25Y Female

FMD検査結果

検査日 2008/11/21 17:28:58 検査者

被検者ID : 05
 氏名 :
 生年月日 :
 性別 :
 メモ :

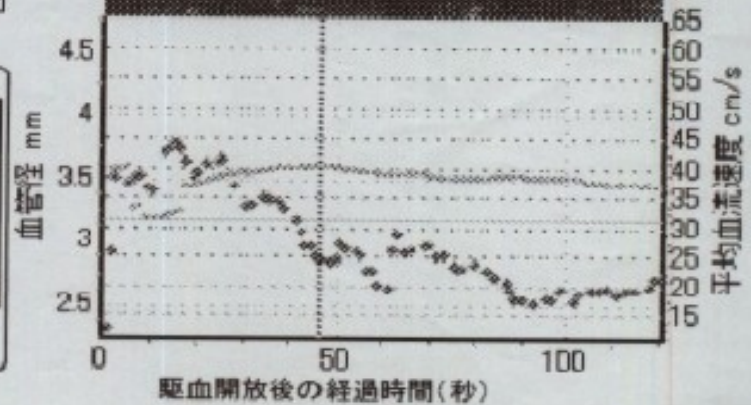
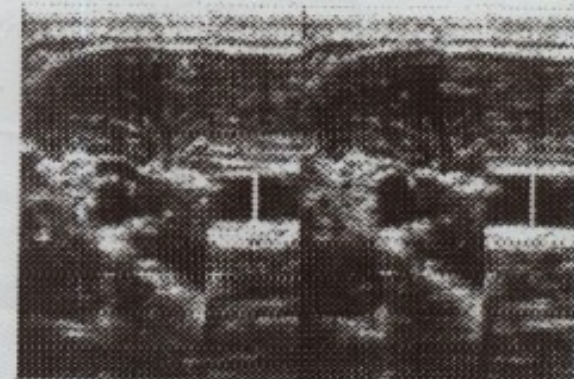
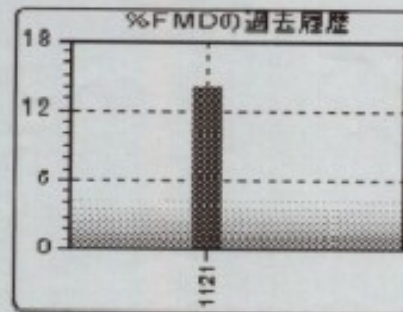
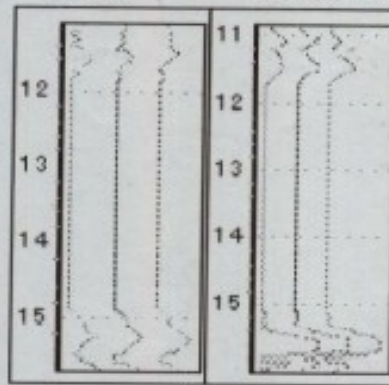
解析結果

FMD値 13.5 %

計測値

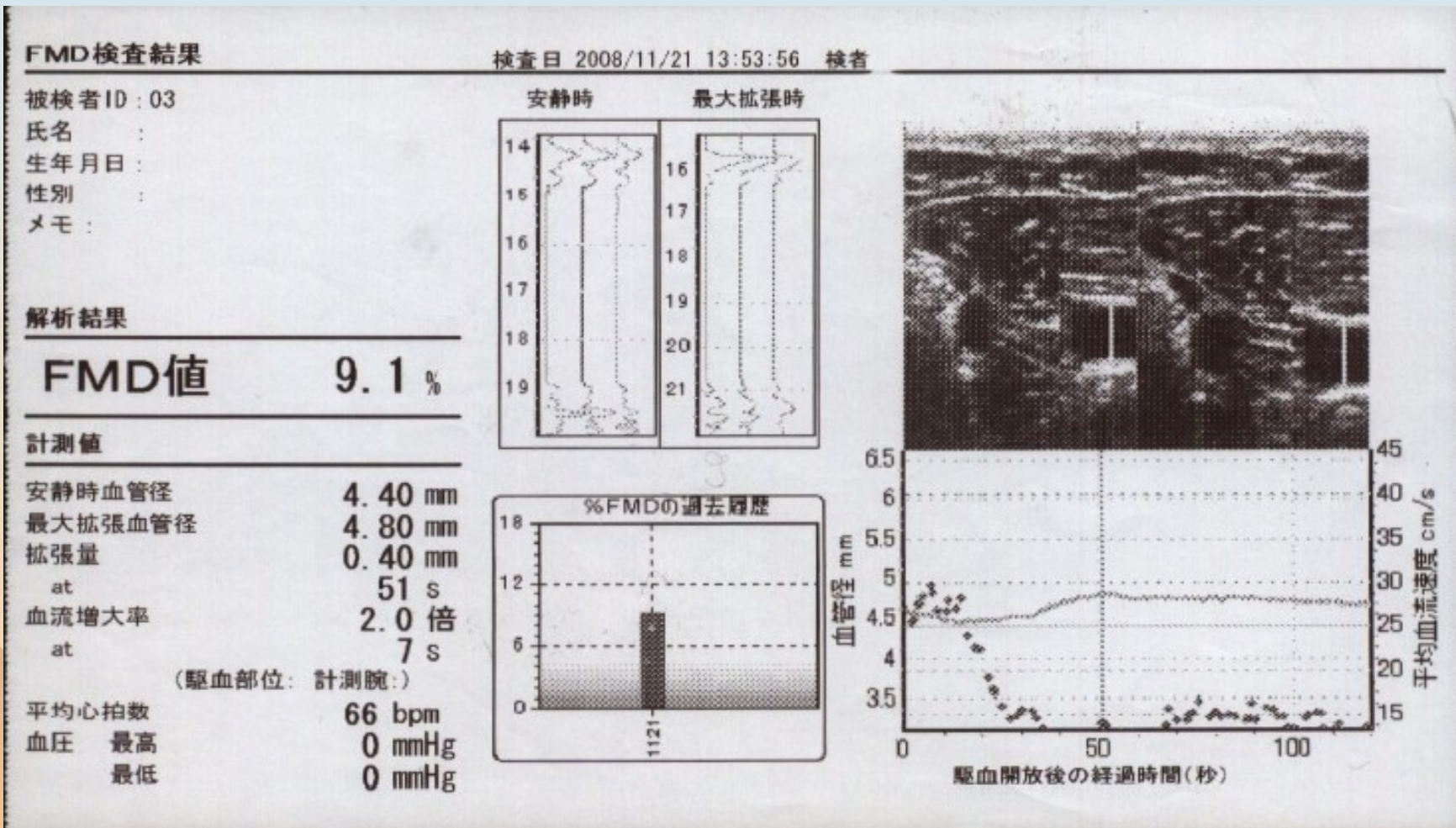
安静時血管径	3.18 mm
最大拡張血管径	3.61 mm
拡張量	0.43 mm
at	46 s
血流増大率	3.5 倍
at	16 s
(駆血部位: 計測腕:)	
平均心拍数	69 bpm
血压 最高	0 mmHg
最低	0 mmHg

安静時 最大拡張時

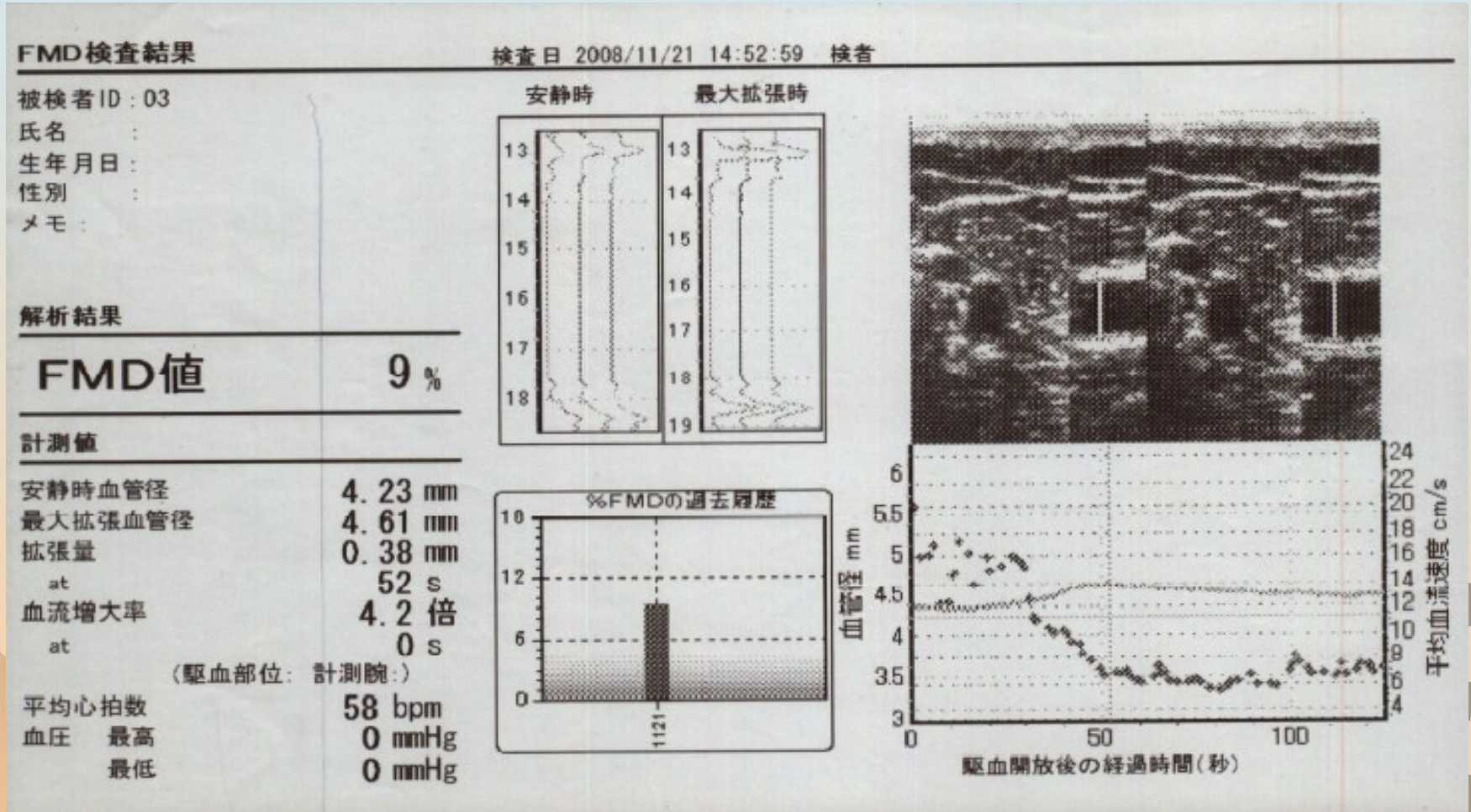


Before MAH

56Y Male



After MAH 56Y Male



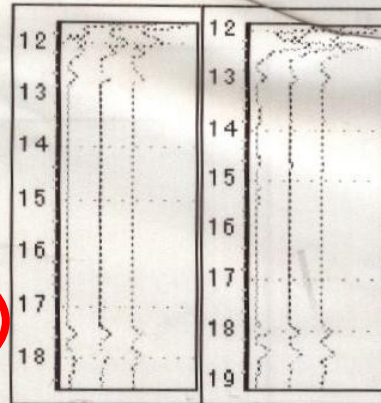
Before MAH 71Y Male

FMD検査結果

検査日 2008/11/21 12:43:27 検者

被検者ID : 02
 氏名 :
 生年月日 :
 性別 :
 メモ :

安静時 最大拡張時

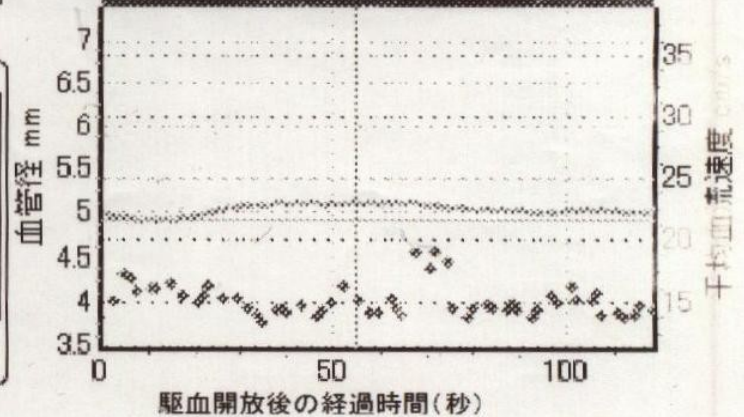
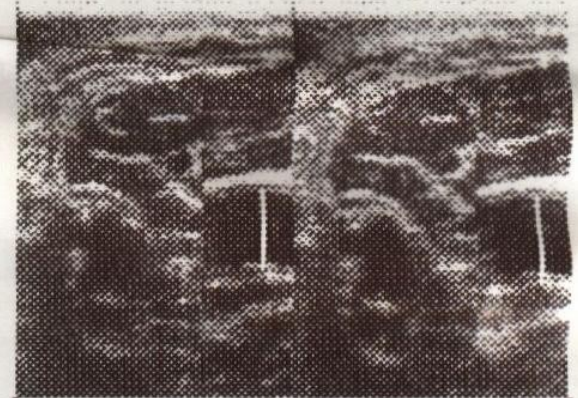
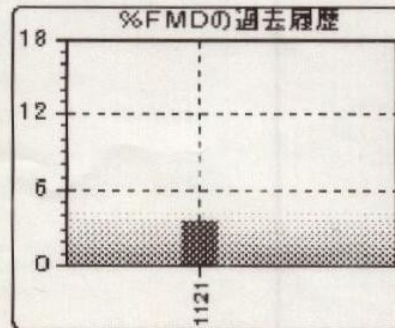


解析結果

FMD値 **3.5 %**

計測値

安静時血管径	4.92 mm
最大拡張血管径	5.09 mm
拡張量	0.17 mm
at	55 s
血流増大率	1.3 倍
at	4 s
(駆血部位: 計測腕:)	
平均心拍数	60 bpm
血压 最高	0 mmHg
最低	0 mmHg



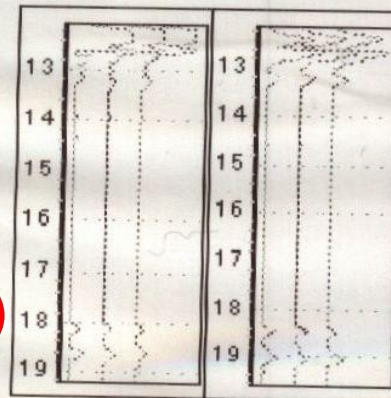
After MAH 7 71Y Male

FMD検査結果

検査日 2008/11/21 13:41:07 検査者

被検者ID: 02
 氏名 :
 生年月日 :
 性別 :
 メモ :

安静時 最大拡張時

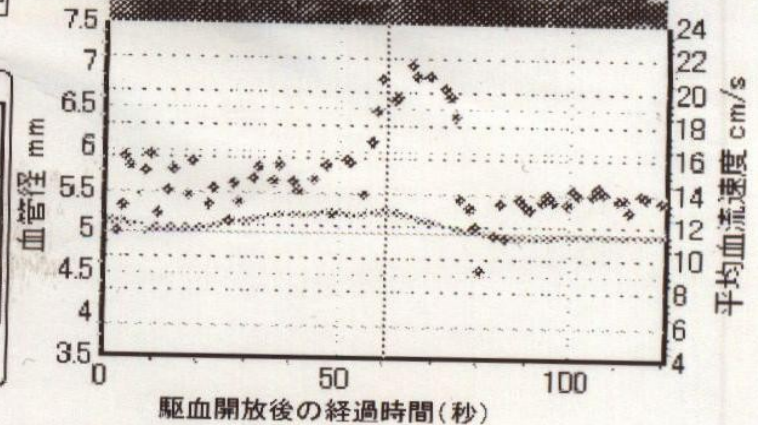
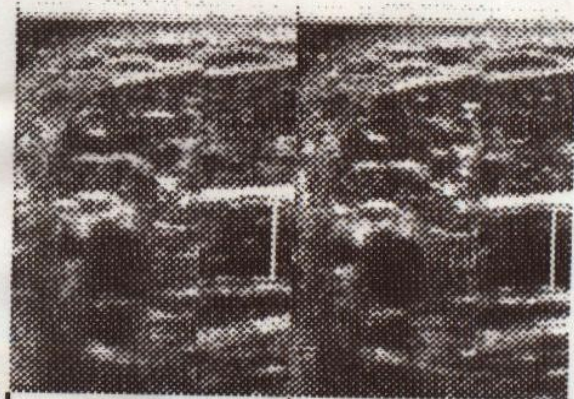
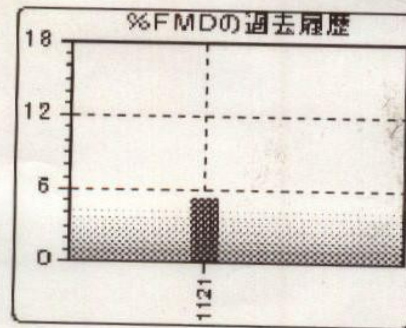


解析結果

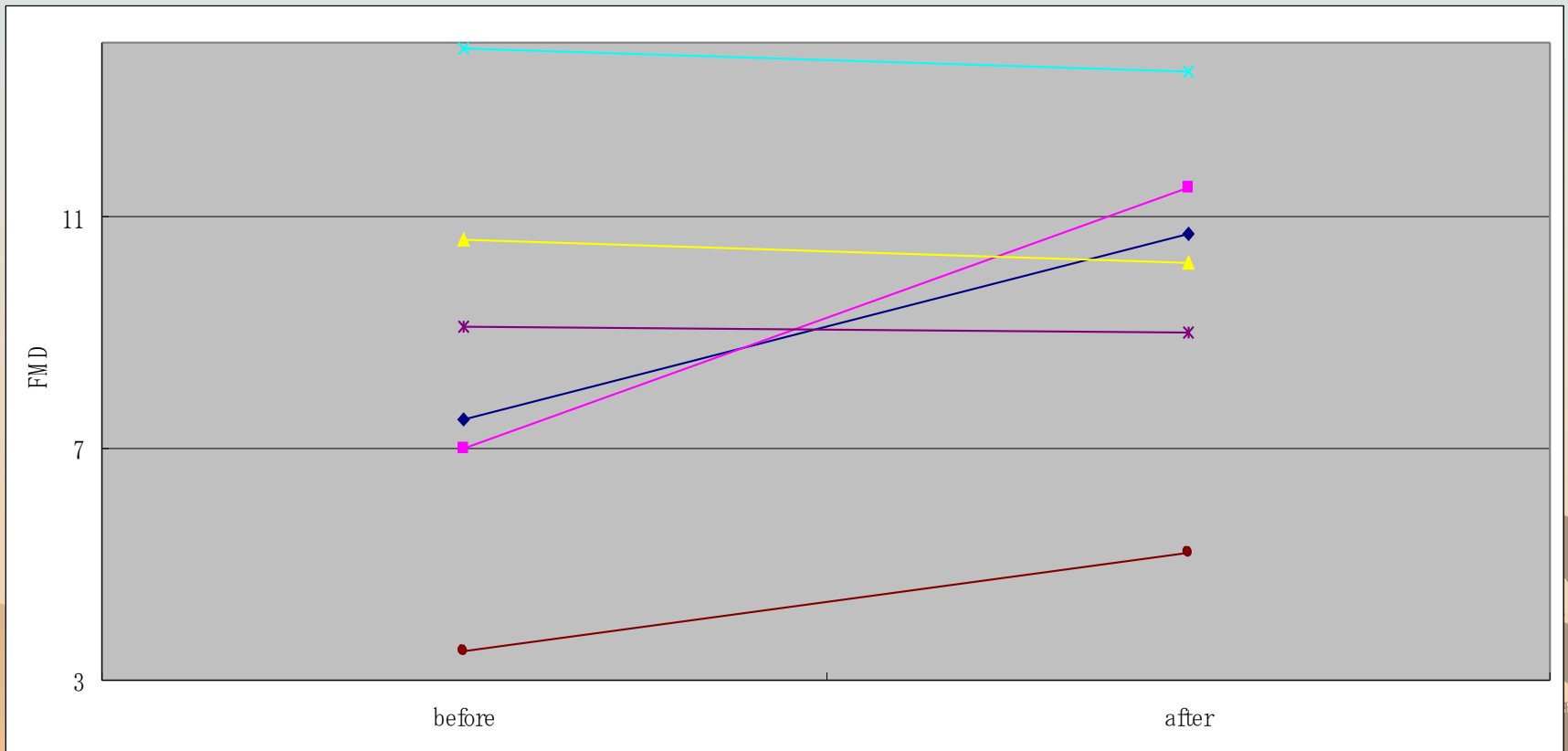
FMD値 **5.2 %**

計測値

安静時血管径 5.00 mm
 最大拡張血管径 5.26 mm
 拡張量 0.26 mm
 at 61 s
 血流増大率 3.3 倍
 at 59 s
 (駆血部位: 計測腕:)
 平均心拍数 57 bpm
 血压 最高 0 mmHg
 最低 0 mmHg

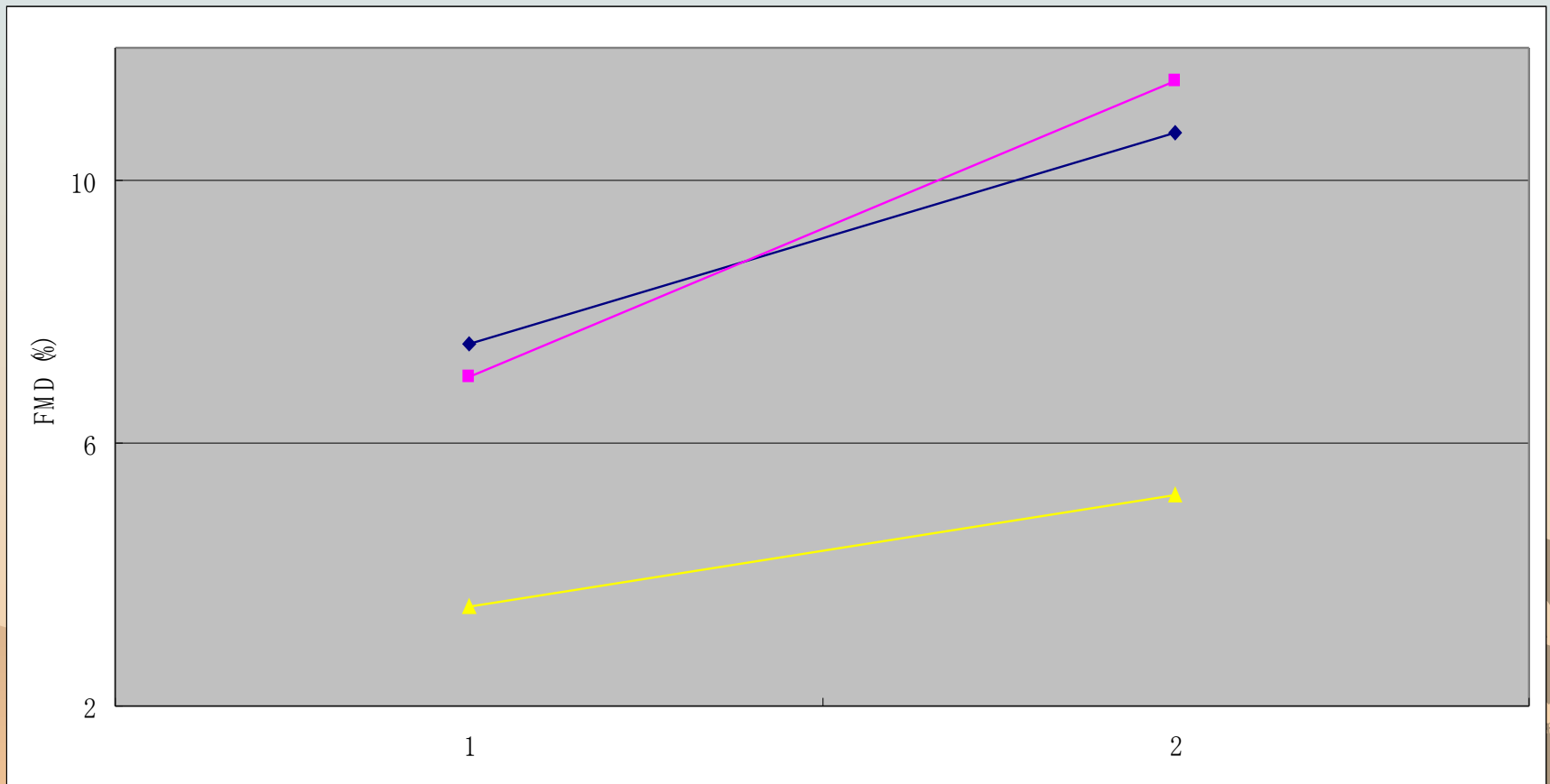


FMD before & after MAH



FMD before & after MAH

(FMD < 8)



FMD

❁ Good FMD → Good prognosis of CVD

❁ Poor FMD → Poor prognosis of CVD

❁ Improvement of FMD

→ improve prognosis?

Persistent Impairment of Endothelial Vasomotor Function Has a Negative Impact on Outcome in Patients With Coronary Artery Disease

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Yamanashi, Japan

Objectives	We assessed the hypothesis that changes in endothelial vasomotor function in response to optimized therapy for atherosclerotic coronary artery disease predict future cardiovascular events.
Background	Although endothelial vasomotor dysfunction is a predictor of cardiovascular events, it remains unclear whether reversibility of endothelial dysfunction in response to risk factor reduction provides prognostic information.
Methods	This study included 251 patients with newly diagnosed coronary artery disease and an impaired flow-mediated dilation (FMD) of the brachial artery (FMD <5.5%). Measurement of FMD was repeated after 6 months for individualized and optimized therapy to reduce risk factors according to American College of Cardiology/American Heart Association guidelines. Patients were followed up for 36 months or until 1 of the following events occurred: cardiac death, nonfatal myocardial infarction, recurrent and refractory angina pectoris requiring coronary revascularization, or ischemic stroke.
Results	FMD was persistently impaired (<5.5%) in 104 (41%) patients after 6 months of optimized therapy, whereas it improved (FMD \geq 5.5%) in the remaining 147 (59%) patients. During 36 months of follow-up, events occurred in 27 (26%) patients with persistently impaired FMD and in 15 (10%) patients with improved FMD ($p < 0.01$ by chi-square test). Multivariate Cox hazards analysis showed that persistent impairment of FMD was an independent predictor of events (hazard ratio: 2.9, 95% confidence interval: 1.5 to 6.2, $p < 0.01$). Baseline FMD before the optimized therapy to reduce risk factor had no significant prognostic information.
Conclusions	Persistent impairment of endothelial vasomotor function despite optimized therapy to reduce risk factors has an adverse impact on outcome in coronary artery disease patients. (J Am Coll Cardiol 2009;53:323–30) © 2009 by the American College of Cardiology Foundation

Endothelial vasomotor dysfunction is an early event identified in the pathogenesis of atherosclerosis (1–4) and is mainly caused by loss of endothelium-derived nitric oxide (EDNO) (5–9). Because EDNO has strong antiatherogenic effects (5,10), endothelial dysfunction is involved in the development of atherosclerotic cardiovascular disease (CVD). Moreover, endothelial vasomotor dysfunction is recognized as a predictor of adverse cardiovascular outcomes

(11–14). However, a decrease in EDNO and endothelial vasomotor dysfunction is reversible after a reduction in atherosclerotic risk factor burden by pharmacological interventions and life-style modifications (15–20). Because a reduction in risk factors improves endothelial vasomotor function, a single assessment of endothelial vasomotor

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function may not necessarily reflect later EDNO activity, and endothelial function measured at a single time point may not reflect long-term progression of atherosclerotic diseases. Most previous studies (12–14) that used endothelial function to predict future cardiovascular events assessed endothelial function at only a single time point; only a few studies evaluated the prognosis based on serial measure-

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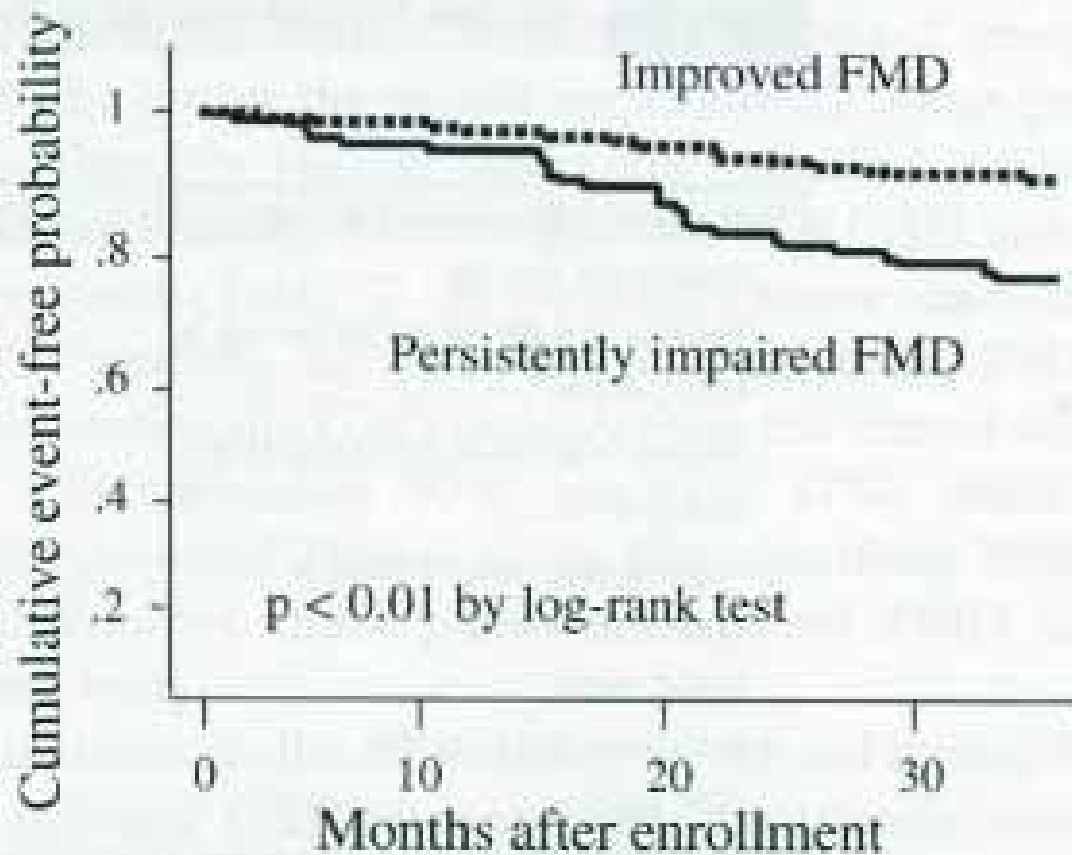
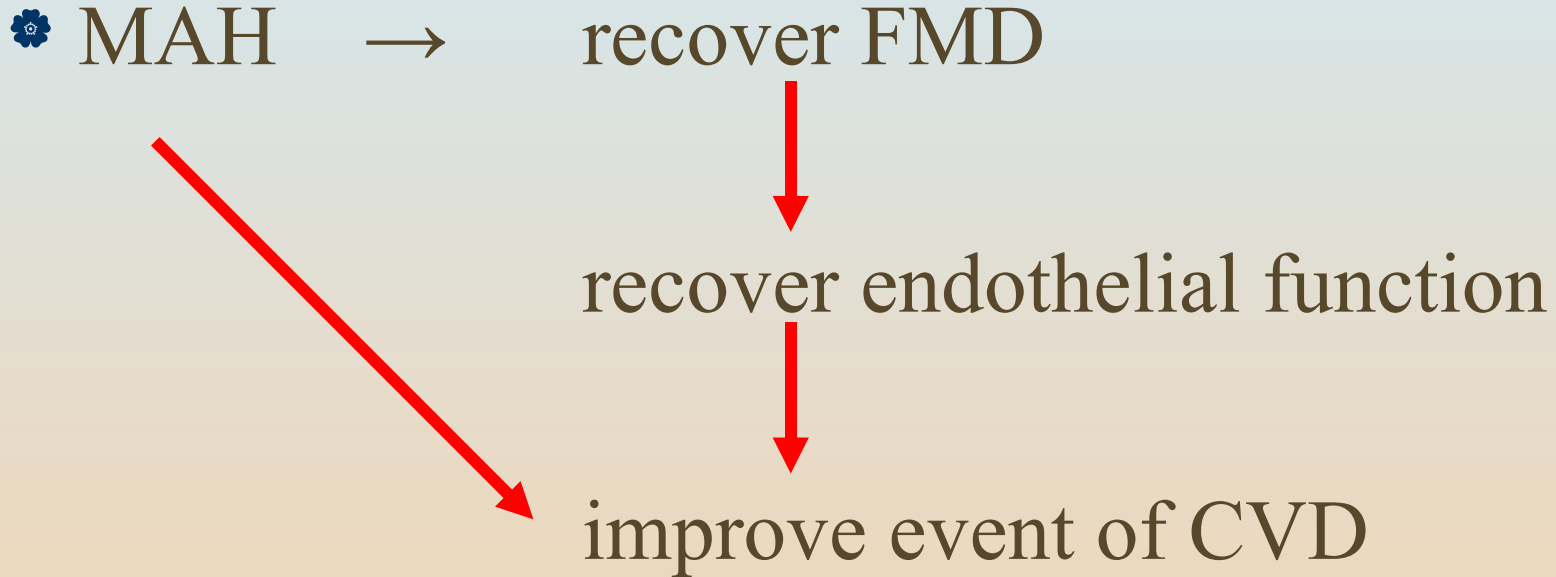


Figure 2 Kaplan-Meier Curves of Event-Free Survival

Kaplan-Meier curves of event-free survival on the basis of change in flow-mediated dilation (FMD) in response to risk factor reduction during the follow-up period (mean, 31 ± 4 months) in 251 patients with coronary artery disease (104 patients had persistently impaired FMD, and 147 patients had improved FMD). The cutoff value ($<5.5\%$) for the impairment of FMD was predetermined from the mean minus 1 SD of FMD in 100 normal subjects in our hospital.

MAH



Today's menu

- ❁ Increase of Antioxidant ability after several MAH (major autohemotherapy)
- ❁ Improvement of Flow Mediated Dilatation even after one MAH
- ❁ Present situation of ozone therapy in Japan
 - MAH, Minor AH, rectal, ozone oil, ozone water

Ozone therapy in Japan

- ❁ Less than 20 clinics
- ❁ Major Autohematotherapy
- ❁ Ozone injection (trigger point, subcutaneous)
- ❁ Ozone olive oil
- ❁ Ozone water

- ❁ Minor Autohematotherapy



Standard protocol in Japan

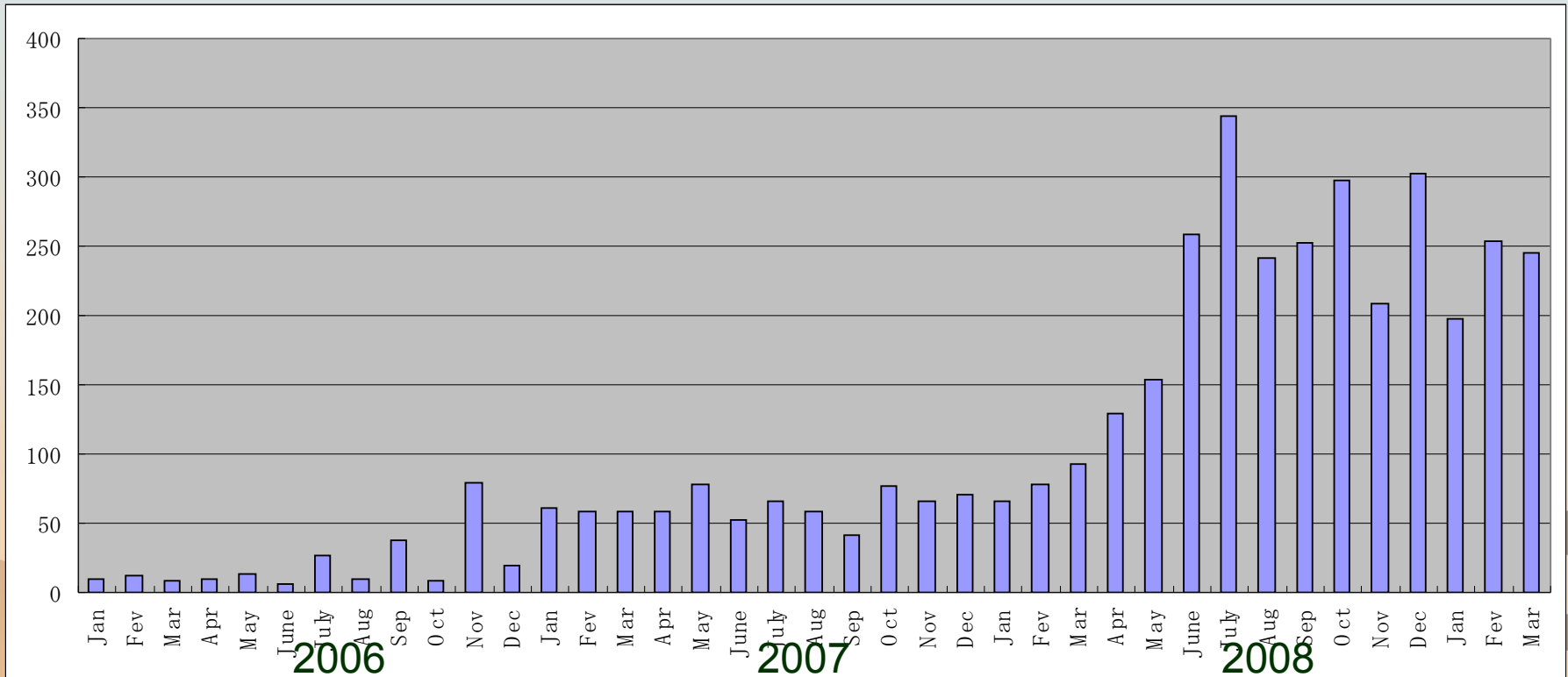
- ❁ 100ml of blood +
50ml of ozone(40mcg/ml)



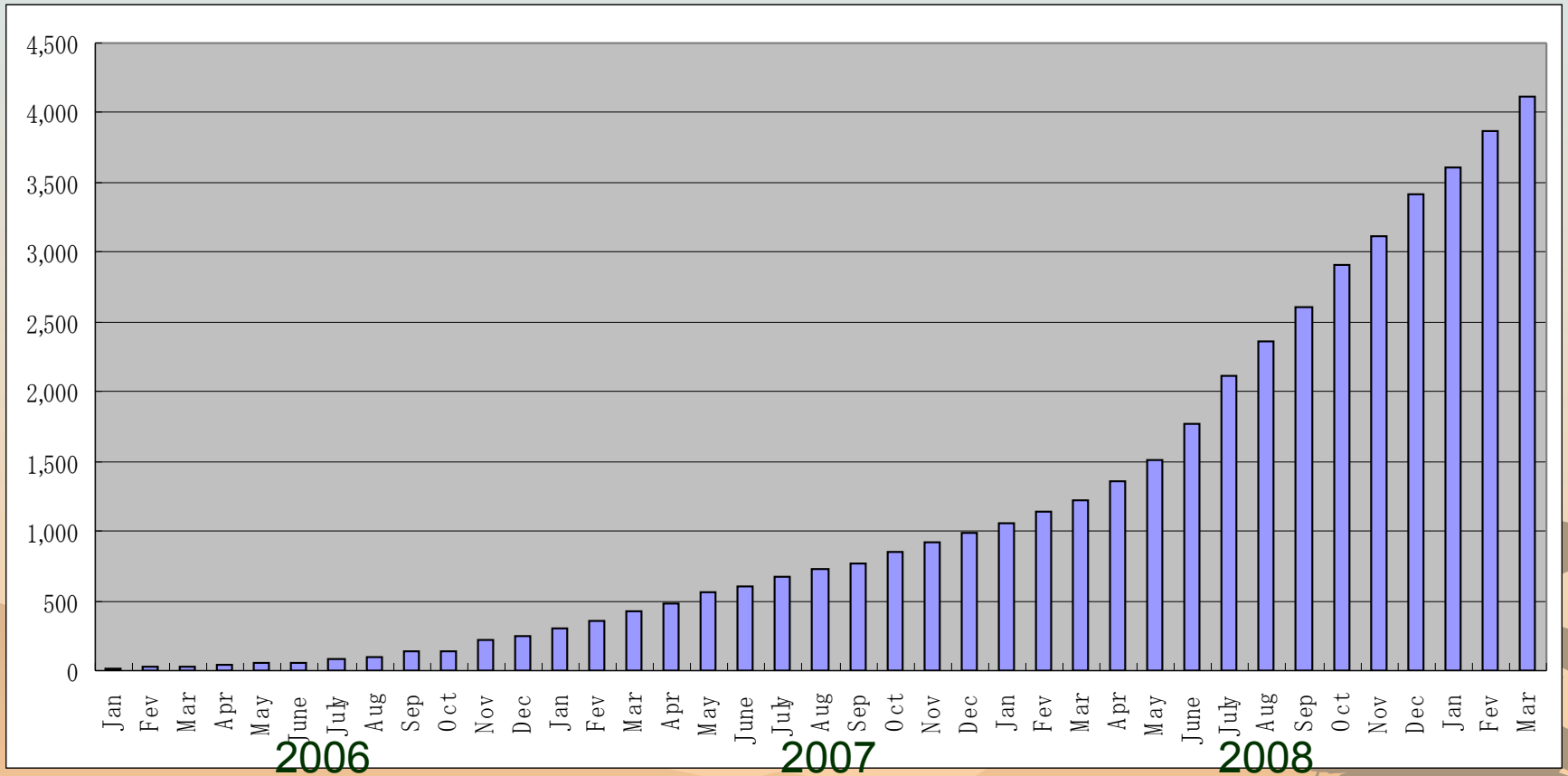
Protocole by our association

	bbod (m l)	ozone (40m cg/m l)	treatm ent #
start dose	100	50	1~2
	100	100	1~5
m aintenance	150	150	

Patient # each month from 2006~2008



Total patient # from 2006~2008



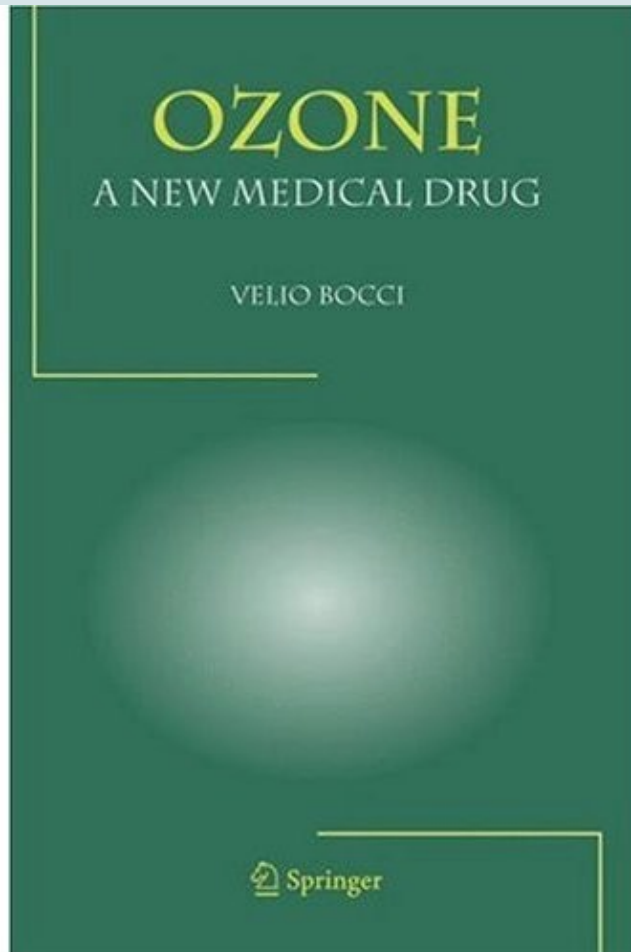
Current endeavors

- ❁ Enlightenment of MAH to Drs and patients
- ❁ Academic research
 - Basic research VS clinical research
- ❁ Japanese Association of ozone therapy
 - President
 - Currently 20 members



OZONE A New Medical Drug

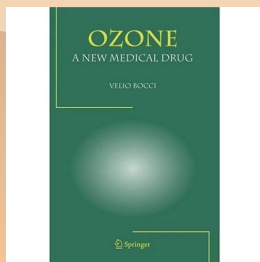
Bocci, Velio



2005, XXVII, 295 p., Hardcover
ISBN: 978-1-4020-3139-7

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