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Title	Power Doppler signal calibration in the finger joint between two models of ultrasound machine: a pilot study using a phantom and joints in patients with rheumatoid arthritis
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Citation	Acta radiologica, 58(10), 1238-1244 https://doi.org/10.1177/0284185116685923
Issue Date	2017-10-01
Doc URL	http://hdl.handle.net/2115/71591
Rights	Sakano, Ryosuke; Saito, Katsumi; Kamishima, Tamotsu; Nishida, Mutsumi; Horie, Tatsunori; Noguchi, Atsushi; Kono, Michihito; Sutherland, Kenneth; Atsumi, Tatsuya; Power Doppler signal calibration in the finger joint between two models of ultrasound machine: a pilot study using a phantom and joints in patients with rheumatoid arthritis, Acta radiologica (Volume 58 Isssue 10) pp.1238-1244. Copyright © 2017. Reprinted by permission of SAGE Publications.
Type	article (author version)
File Information	Acta radiologica_58 (10) _1238-1244.pdf

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Power Doppler signal calibration in the finger joint between two models of ultrasound machine: a pilot study using a phantom and joints in patients with rheumatoid arthritis

Short title; Power Doppler signal calibration for rheumatoid arthritis

Abstract

Background: Despite the advantages of ultrasound (US) in the management of rheumatoid arthritis (RA) patients, power Doppler (PD) US may be highly dependent on the type of US machine used.

Purpose: To present a method to calibrate the PD signal of two models of US machines by use of a flow phantom and finger joints of patients with RA.

Material and Methods: For the phantom study, the PD signal count was measured in the flow phantom perfusing blood mimicking fluid at various injection rates and pulse repetition frequencies (PRFs). The quantitative PD index was calculated with ImageJ. For the clinical study, the 2nd and 3rd metacarpophalangeal joints of five consecutive patients with RA were examined. The quantitative PD index was measured at various PRFs by use of two models of machine (the same models as the phantom study).

Results: For the phantom and clinical studies, negative correlations were found between the PRF and the quantitative PD index when the flow velocity was constant and positive correlations between flow velocity and the quantitative PD index at constant PRF. There was a significant difference in the depiction performance of synovial blood flow between the two models, which can be calibrated by adjusting the PRF values derived from the phantom study in each model.

Conclusion: Signal calibration of pannus vascularity between US machines may be possible by adjusting the PRF value according to flow phantom data. Different US machines can thus provide equivalent examination results concerning the pannus vascularity.

Keywords:

power Doppler; signal calibration; finger joint; phantom; rheumatoid arthritis

Introduction

Ultrasound (US) can depict soft tissue hyperemia in musculoskeletal inflammatory disease (1) and allows a sensitive detection of synovitis (2). Disease activity and treatment response may be estimated by power Doppler (PD) US in RA patients (3). Despite the advantages of US in the management of RA patients, PDUS may be highly dependent on the type of US machine used (4), as there are significant machine-to-machine disagreements for signal quantification (5, 6).

The sensitivity of PD is affected by factors and parameters such as machine specification, deterioration of the transducer, transmit frequency, Doppler gain, pulse repetition frequency (PRF), and wall filter adjustments. All of these factors and parameters are source of disagreement for PD sensitivity, however, they may conversely be potential candidates for calibration of PD signal quantification between different US systems.

We previously demonstrated that the signal calibration of various models of US machines is possible by adjustment of the PRF setting utilizing the relationship between PRF and quantitative PD (7, 8). However, a limitation of previous studies (7, 8) is the use of normal saline and microbubbles as the perfusion solution. Conclusions drawn from microbubbles have to be handled very carefully due to the influence of bubble cavitation. To solve this problem, it is necessary to use a flow phantom for PD quantification using blood mimicking fluid (6, 9) which is not affected by bubble cavitation.

In this study, we hypothesize that we can calibrate the PD signal in the finger joints of two US models using a flow phantom with blood mimicking fluid, so that the two models can provide equivalent examination results concerning pannus vascularity. The relationship between the PRF, the quantitative PD index and the flow velocity on each machine was first analyzed using a phantom. A similar method was then applied and validated in the clinical situation.

Material and Methods

Phantom study

The positive PD signal count was measured at various injection rates (flow velocity) and PRFs. A flow phantom (Hemodialyzer FLX-18GW, Nikkiso Co., Ltd., Tokyo, Japan) in a tub filled with water was connected to an angiography injector PRESS PRO (Nemoto Kyorindo, Tokyo, Japan), and blood mimicking fluid (6, 9) was injected with similar settings in previous studies.

Two US machine models were used; Avius (HITACHI Aloka, Tokyo, Japan) and LOGIQ E9 (GE Healthcare, Piscataway, NJ, USA.). For Avius, using a linear probe 6-14MHz, PRFs (500, 650, 800, 1000, and 1300Hz) at preset were adjusted: FINGER, depth: 1.75 cm, color focus: 1 cm, Doppler gain: 40, color flow mapping filter: M, transmit power: 1.0, frame rate: 8-10. During quantitative PD measurements, the probe was located parallel to the flow direction in the phantom. For maximum flow velocity measurement, the probe was placed at 50 degrees to the flow direction. For LOGIQ E9, using a linear probe, ML6-15, PRFs (600, 800, 1000, 1200, and 1500Hz) at preset were adjusted: MSK superficial, depth: 2.75 cm, color focus: 1.5 cm, Doppler gain: 15, transmit power: 0.4, frame rate: 10. For both models, the level of wall filter was automatically determined according to PRF settings by linked controls. The transmit frequencies were 7.5 MHz for Avius and 15 MHz for LOGIQ.

The PRF setting as described above was selected because PRFs beyond these are not used in clinical situations. Here, the usage of "PRF" is not universally defined, but only a parameter value defined by the manufacturer.

The injection rate of the angiography injector was set to 1.2, 1.5, 1.8, 2.1, and 2.4 ml/s because we were interested in the flow depiction of the US machine at low injection rates or slow flow. The flow velocity was measured in the perfusion cartridge at various injection rates (1.2-2.4 ml/s) at a constant PRF of 1000Hz by using the Doppler spectral analysis of the Avius.

The capillary flow phantom was modified as proposed by Veltmann et al. (10). The flow phantom contained 10,000 tubes with an inside diameter of 210 μ that were distributed equally over the whole cross-sectional area of the phantom (7, 8). The blood mimicking fluid entered the capillaries at the entry chamber, streamed through and left the capillaries from the exit chamber at the other end of the phantom. There were no confounding Doppler signals from bubbles in other phantom fluids or vessel-wall motion by perfusing the phantom with normal saline.

Doppler signals at flow rates of 1.2, 1.5, 1.8, 2.1, and 2.4 ml/sec were examined for maximum flow velocity in the Avius, which was calculated automatically on a console by tracing the velocity line developed by spectral Doppler sonography. From movie data obtained in phantom experiments at various flow rates and PRF settings, a sonographer selected one still image for each experiment and measured the quantitative PD index (the summation of the colored pixels in a 0.5 cm × 1 cm rectangular region of interest (ROI)) using ImageJ (https://imagej.nih.gov/ij/). Still images were selected when the flow signal was stable and free of artifacts. Each measurement was performed three times, and the mean value for the quantitative PD index was calculated.

Clinical study

This study was conducted in accordance with the Declaration of Helsinki and approved by the local ethics committee. All patients were diagnosed with RA according to the American College of Rheumatology (1987) criteria (11). The inclusion criteria of this arthritis cohort consisted of active arthritis, based on clinical findings, of at least the wrist, or finger joint, but without the knowledge of the extent of the disease. All patients who were managed in a dedicated rheumatology ward in a university hospital were assessed for continuation/cessation of the biological treatment or for switching to an alternative biological agent. All subjects were recruited from consecutive patients admitted to the university hospital. Ethics board permission and written informed patient consent were obtained for this study. The 2nd and 3rd metacarpophalangeal (MCP) joints of both hands in 5 consecutive RA patients (4 females and 1 male) were included in this study (Table 1).

Images were obtained following the Guidelines for musculoskeletal US in rheumatology (12) at room temperature of 24 degrees centigrade. The positive PD signal count was measured at various PRFs with the same models and by the same radiological technologist as the phantom study. Two US machine models were used; Avius (HITACHI Aloka, Tokyo, Japan) and LOGIQ E9 (GE Healthcare, Piscataway, NJ, USA.). For Avius, using a linear probe 6-14MHz, PRFs (500, 650, 800, 1000, and 1300Hz) at preset were adjusted: FINGER, color flow mapping filter: M, transmit power: 1.0, frame rate: 8-10. For LOGIQ E9, using a linear probe, ML6-15, PRFs (600, 800, 1000, 1200, and 1500Hz) at preset were adjusted: MSK superficial, transmit power: 0.4, frame rate: 10. For both machines, PDUS was performed by single view mode, the horizontal width of the ROI was set to full screen, and Doppler gain was kept stable at 38-40 for Avius and 20 for LOGIQ E9.

In the semi-quantitative grading assessment, still images with various PRF settings of the two US machine models were randomly assigned and then evaluated by one radiological technologist with more than 10 years' experience in joint ultrasonography. Each evaluation was performed three times. The value by majority vote was applied out of the three semi-quantitative grading results for each image. For interobserver repeatability assessment, one medical technologist with more than 10 years' experience in joint ultrasonography graded the same images. A semi-quantitative grading system defined by Szkudlarek et al. (grade 0 = no flow in the synovium, grade 1

= single vessel signals, grade 2 = confluent vessel signals in less than half of the area of the synovium, grade 3 = vessel signals in more than half of the area of the synovium) was used (13).

The quantitative PD index (the summation of the colored pixels in the MCP joint in a manually defined ROI) of fifty still images was measured using ImageJ. Each measurement was performed three times, and the mean value for the quantitative PD index was applied.

Statistical analysis

Statistical analyses were performed with the use of Microsoft Excel 2010, and PASW Statistics 22. Correlations between two variables were examined with the use of a parametric test (Pearson's correlation test). The intraobserver US agreement was calculated using unweighted Coohen's kappa. The Kappa value measures agreement between pairs of observers, eliminating random concordance. A Kappa value was translated as 0 representing less than chance agreement, 0.01–0.20 slight agreement, 0.21–0.40 fair agreement, 0.41–0.60 moderate agreement, 0.61–0.80 substantial agreement and 0.80–0.99 almost perfect agreement.

Results

Phantom study

A positive correlation was found between injection rate and flow velocity when the PRF was constant with a correlation coefficient of 0.9969.

For Avius, negative correlations were found between the PRF and the quantitative PD index when the flow velocity was constant (correlation coefficient of -0.9549 ± 0.02258 (-0.9220 to -0.9852) for the mean ± SD (range), $p<0.05$) (Fig.1a), and positive correlations between flow velocity and the quantitative PD index at a constant PRF (correlation coefficient of 0.9544 ± 0.03851 (0.8880 to 0.9915) for mean ± SD (range), $p<0.05$) (Fig.1a).

For LOGIQ E9, negative correlations were found between the PRF and quantitative PD index (only at 2.1, 2.4 ml/s flow velocity) when the flow velocity was constant (correlation coefficient of -0.9123 ± 0.004259 (-0.9081 to -0.9166) for mean ± SD (range), $p<0.05$) (Fig.1b), and positive correlations between flow velocity and the quantitative PD index (except at 1500Hz PRF) at a constant PRF (correlation coefficient of 0.9268 ± 0.01505 (0.9089 to 0.9503) for mean ± SD (range), $p<0.05$) (Fig.1b).

For both US machine models, negative correlations were found between the PRF and the quantitative PD index when the flow velocity was constant and positive correlations between the flow velocity and the quantitative PD index at a constant PRF.

Further, a conversion formula of the relationship of the PRF between Avius and LOGIQ E9 was created using an equation of the relationship between the PRF and the quantitative PD index of each machine (approximate expression) in 2.1, 2.4 ml/s flow velocity, where negative correlations were found between the PRF and the quantitative PD index: $y = 0.3656x + 983.7$ (x = PRF of LOGIQ E9 [Hz], y = PRF of Avius [Hz]) (Fig.2).

Clinical study

For the intraobserver US agreement, the unweighted kappa value showed a good correlation (kappa value = 0.78), while interobserver US agreement represented a moderate correlation (kappa value = 0.418).

Positive signals for pannus vascularity were observed at 5 MCP joints in 2 subjects out of 20 MCP joints of 5 subjects. Tables 2 and 3 show the results of the semi-quantitative grading assessment for joints with positive Doppler signals. For Avius, the results of the grading score changed with PRF adjustment at one in five MCP joints.

For LOGIQ E9, the results of the grading score changed with PRF adjustment at two in five MCP joints. Further, the results of the grading score were different between Avius and LOGIQ E9 in the preset PRF.

Figs. 3a and 3b show the results of the quantitative assessment for joints with positive Doppler signals. For Avius, negative correlations were found between the PRF and the quantitative PD index at all MCP joints (correlation coefficient of -0.9777 ± 0.01810 (-0.9454 to -0.9969) for the mean ± SD (range), $p<0.05$) (Fig.3a). For LOGIQ E9, negative correlations were found between the PRF and the quantitative PD index at all MCP joints (correlation coefficient of -0.9788 ± 0.02023 (-0.9423 to -0.9951) for the mean ± SD (range), $p<0.05$) (Fig.3b). Although the quantitative PD index of LOGIQ E9 was lower than that of Avius, there was overlap between the PRF of Avius and LOGIQ E9. A relationship of PRF were also found between Avius and LOGIQ E9 (Fig. 2). This was generally in concordance with the results of the phantom study (Fig.2). An example of difference in image appearance, grading score, and quantitative PD index due to variable PRF values for Avius (HITACHI Aloka) and LOGIQ E9 (GE) is displayed in Fig. 4.

For 15 MCP joints of 4 subjects, no flow signal was detected at any PRF settings of the two US systems.

Discussion

The utility of US in rheumatic diseases is recognized worldwide, and PDUS is becoming a powerful tool for clinicians dealing with patients with RA. However, the lack of standardization of machine settings prevents the production of reliable evidence produced via multicenter trials. This may be a fundamental issue in addition to the choice of grading system when considering the conduction of a clinical trial.

In this study, a method to calibrate the PD signal of two models of US machine was developed by use of a flow phantom with blood mimicking fluid. Furthermore, the difference in the depiction of performance between these machines in application to PD ultrasonography in RA patients was clarified.

For the phantom study, a relationship was demonstrated between signal counts from the two US machines by a simple equation, using the PRF as a variable. The sensitivity of the PD is affected by the PRF adjustments. Generally, when a high PRF is chosen, it is assumed that the investigator is interested in high velocities of the pannus vascularity, and therefore filters that remove low flow to eliminate noise are applied (so-called linked controls). Selecting a high PRF therefore makes the system insensitive to lower velocities because of the linked controls (14). However, the direct cause of the negative correlation between the PRF and the quantitative PD index cannot be determined because the linked controls are differently implemented for each US system.

For the clinical study, although there is a considerable difference in depiction performance of synovial blood flow between Avius and LOGIQ E9, a relationship of the PRF between Avius and LOGIQ E9 was found. This was generally in concordance with the results of the phantom study. For the PRF setting in this study, the results of the grading score changed as a result of PRF adjustment at one in five MCP joints for Avius, and two in five MCP joints for LOGIQ E9. Negative correlations were also found between the PRF and the quantitative PD index in quantitative assessment. For the turning point of the grade evaluation in the semi-quantitative assessment, there is a possibility that PRF adjustment affects the evaluation for pannus vascularity. This concern is highlighted when considering our modest interobserver US agreement (kappa value = 0.418) compared with those of 0.6-0.8 in previous studies (13, 15).

Furthermore, a different quantitative PD index was found by PRF setting adjustment in the quantitative assessment even though the grading score was the same. This poses an obstacle to conducting a multi-center investigation, for example, of the treatment effect of a newly developed therapeutic agent by the use of US. We suggest that a calibration tool be introduced between different US systems, followed by quantitative metrics rather than semi-quantitative grading for multi-center investigation.

There are a few limitations to this study. The fine and complex fractal structure of the vessel tree in vivo could not be simulated by our approach. However, the purpose of this study was to evaluate the possibility of the calibration of the flow signal, but was not confined to the signal purely from the flow of the capillary velocity. The combination of the parameter settings such as depth, focus, and gain were different between the systems in both phantom and clinical studies. The rationale in using different settings for different machines lies in the fact that the first priority of the various parameter settings is to maximize the detection ability of the flow signal.

In conclusion, signal calibration of pannus vascularity between US machines may be possible by adjusting the PRF value according to the flow phantom data. The different US machines can thus provide equivalent examination results concerning the pannus vascularity.

References

1. Newman JS, Adler RS, Bude RO, et al. Detection of soft-tissue hyperemia: value of power Doppler sonography. Am J Roentgenol 1994;163:385-389.

2. Backhaus M, Kamradt T, Sandrock D, et al. Arthritis of the finger joints: a comprehensive approach comparing conventional radiography, scintigraphy, ultrasound, and contrast-enhanced magnetic resonance imaging. Arthritis Rheum 1999;42:1232-1245.

3. Newman JS, Laing TJ, McCarthy CJ, et al. Power Doppler sonography of synovitis: assessment of therapeutic response--preliminary observations. Radiology 1996;198:582-584.

4. Browne JE, Watson AJ, Hoskins PR, et al. Validation of a sensitivity performance index test protocol and evaluation of colour Doppler sensitivity for a range of ultrasound scanners. Ultrasound Med Biol 2004;30:1475-1483.

5. Albrecht K, Grob K, Lange U, et al. Reliability of different Doppler ultrasound quantification methods and devices in the assessment of therapeutic response in arthritis. Rheumatology (Oxford) 2008;47:1521-1526.

6. Koski JM, Saarakkala S, Helle M, et al. Power Doppler ultrasonography and synovitis: correlating ultrasound imaging with histopathological findings and evaluating the performance of ultrasound equipments. Ann Rheum Dis 2006;65:1590-1595.

7. Kamishima T, Nishida M, Horie T, et al. Power Doppler signal calibration using capillary phantom for pannus vascularity in rheumatoid finger joint. A pilot study. Clin Exp Rheumatol 2011;29:1057.

8. Sakano R, Kamishima T, Nishida M, et al. Power Doppler signal calibration between ultrasound machines by use of a capillary-flow phantom for pannus vascularity in rheumatoid finger joints: a basic study. Radiol Phys Technol 2015;8:120-124.

9. Ramnarine KV, Nassiri DK, Hoskins PR, et al. Validation of a new blood-mimicking fluid for use in Doppler flow test objects. Ultrasound Med Biol 1998;24:451-459.

10. Veltmann C, Lohmaier S, Schlosser T, et al. On the design of a capillary flow phantom for the evaluation of ultrasound contrast agents at very low flow velocities. Ultrasound Med Biol 2002;28:625-634.

11. Chogle AR, Desai BH, Jhankaria GR. American Rheumatism Association 1958 and 1987 revised criteria for rheumatoid arthritis--how useful to the clinician. J Assoc Physicians India 1996;44:93-97.

12. Backhaus M, Burmester GR, Gerber T, et al. Guidelines for musculoskeletal ultrasound in rheumatology. Ann Rheum Dis 2001;60:641-649.

13. Szkudlarek M, Court-Payen M, Jacobsen S, et al. Interobserver agreement in ultrasonography of the finger and toe joints in rheumatoid arthritis. Arthritis Rheum 2003;48:955-962.

14. Torp-Pedersen ST, Terslev L. Settings and artefacts relevant in colour/power Doppler ultrasound in rheumatology. Ann Rheum Dis 2008;67:143-149.

15. Kamishima T, Tanimura K, Henmi M, et al. Power Doppler ultrasound of rheumatoid synovitis: quantification of vascular signal and analysis of interobserver variability. Skeletal Radiol 2009;38:467-472.

Tables

Table 1 Baseline patient characteristics

Patient	Age (years)	Sex	Disease duration (months)	DAS28-ESR score
1	59	M	24	5.17
2	67	F	204	5.44
3	62	F	18	3.25
4	38	F	15	4.89
5	60	F	179	4.44

DAS28-ESR score, Disease Activity Score in 28 joints calculated with erythrocyte sedimentation rate

Table 2 Grading score of Avius in clinical study

Patient	Joint	PRF [Hz]				
		500	650	800*	1000	1300
1	LT-MCP2	2	2	2	2	2
2	RT-MCP2	3	3	2	2	2
	RT-MCP3	2	2	2	2	2
	LT-MCP2	2	2	2	2	2
	LT-MCP3	2	2	2	2	2

* , preset

MCP, metacarpophalangeal joint

Table 3 Grading score of LOGIQ E9 in clinical study

Patient	Joint	PRF [Hz]				
		600	800*	1000	1200	1500
1	LT-MCP2	2	2	1	1	1
2	RT-MCP2	2	2	2	2	2
	RT-MCP3	2	2	2	2	2
	LT-MCP2	2	2	2	2	2
	LT-MCP3	2	2	2	2	2

* , preset

MCP, metacarpophalangeal joint

Figure Legends

Fig.1a. Avius (HITACHI Aloka) in the phantom study, the relationship between the PRF (Hz) and the QPD index (%) with variable flow velocity.

Fig.1b. LOGIQ E9 (GE) in the phantom study, the relationship between the PRF (Hz) and the QPD index (%) with variable flow velocity.

PRF, pulse repetition frequency; QPD index, quantitative power Doppler index

Fig.2. Relationship of the PRF between Avius (HITACHI Aloka) and LOGIQ E9 in the phantom and clinical study.

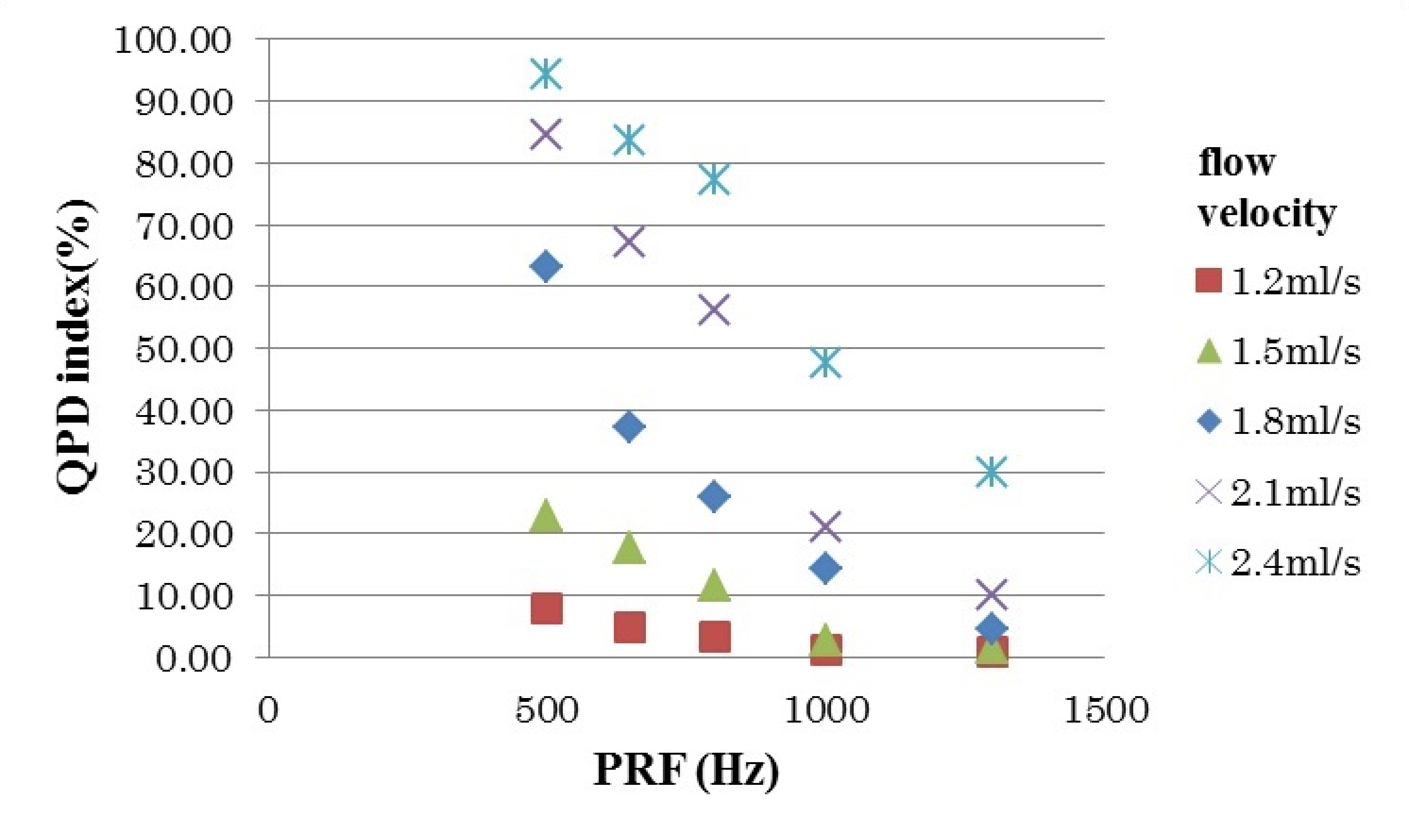
PRF, pulse repetition frequency; MCP, metacarpophalangeal joint

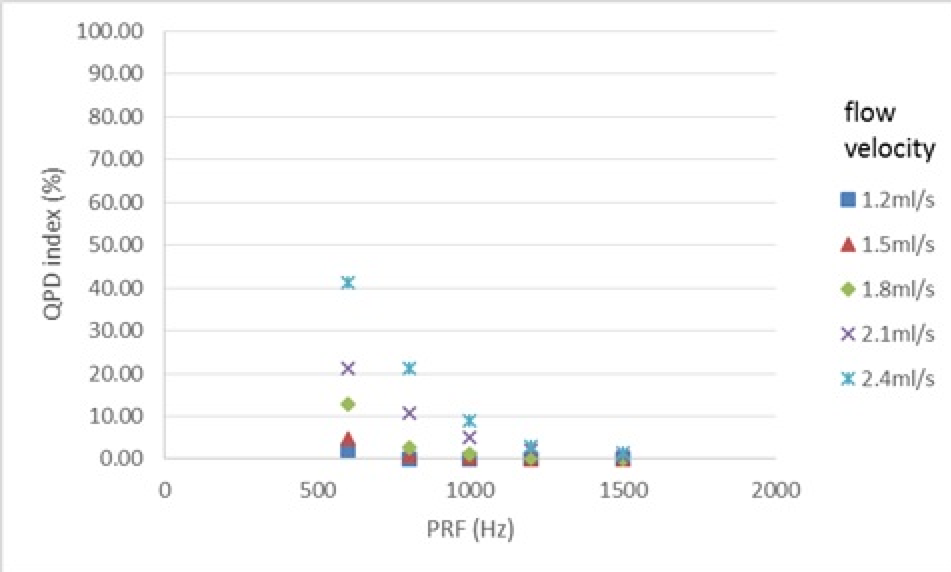
Fig.3a. Avius (HITACHI Aloka) in the clinical study, the relationship between the PRF (Hz) and the QPD index (%).

Fig.3b. LOGIQ E9 (GE) in the clinical study, the relationship between the PRF (Hz) and the QPD index (%)

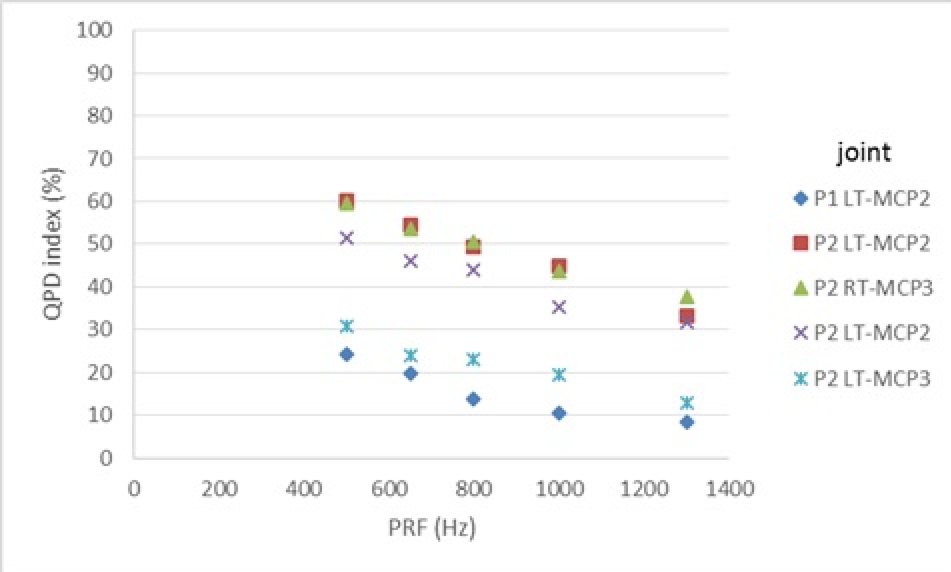
PRF, pulse repetition frequency; QPD index, quantitative power Doppler index; MCP, metacarpophalangeal joint

Fig.4. Difference in image appearance, grading score, and QPD index due to variable PRF values on Avius (HITACHI Aloka) and LOGIQ E9 (GE) in the 2nd MCP joint of the right hand in a 67 year old woman with rheumatoid arthritis

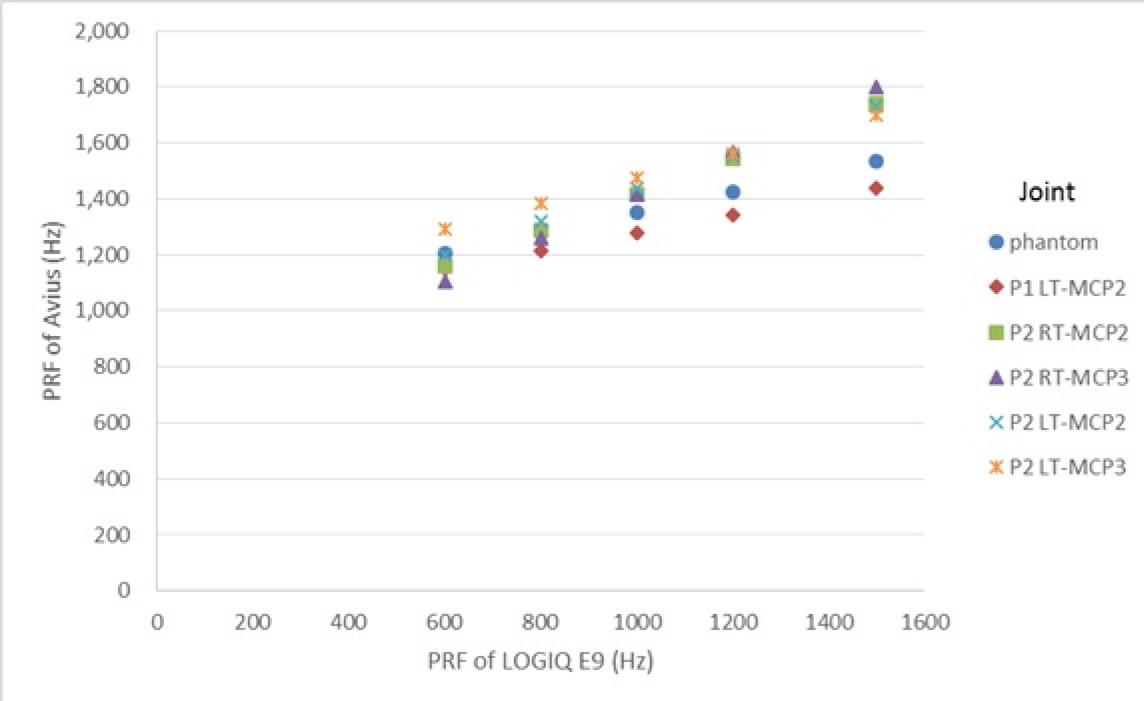

QPD index(%)
100.00
90.00
80.00
70.00
60.00
50.00
40.00
30.00
20.00
10.00
0.00
0
500
1000
1500
PRF (Hz)
flow velocity
1.2ml/s
1.5ml/s
1.8ml/s
2.1ml/s
2.4ml/s



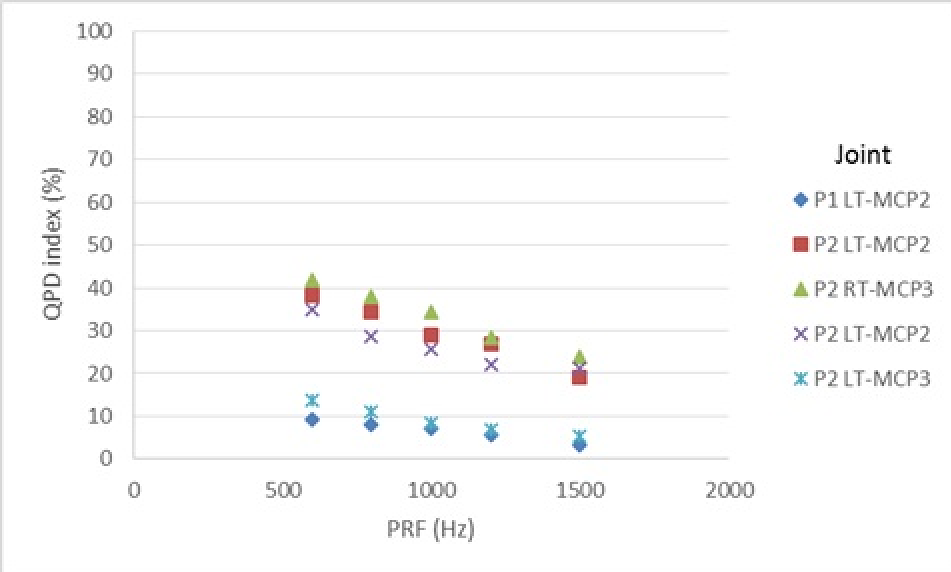
100.00
90.00
80.00
70.00
60.00
50.00
40.00
30.00
20.00
10.00
0.00
QPD index (%)
0
500
1000
1500
2000
PRF (Hz)
flow velocity
1.2ml/s
1.5ml/s
1.8ml/s
2.1ml/s
2.4ml/s



100
90
80
70
60
50
40
30
20
10
0
QPD index (%)
0
200
400
600
800
1000
1200
1400
PRF (Hz)
joint
P1 LT-MCP2
P2 LT-MCP2
P2 RT-MCP3
P2 LT-MCP2
P2 LT-MCP3

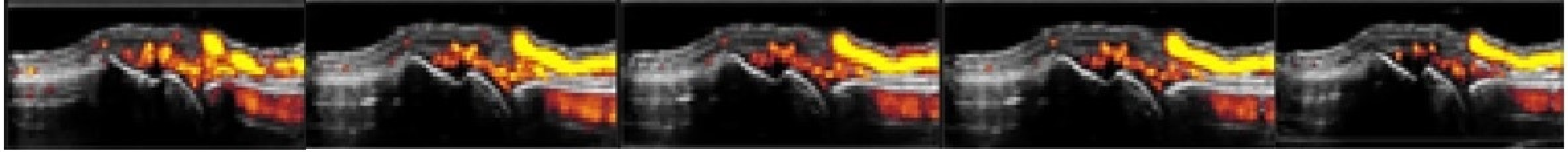


2,000
1,800
1,600
1,400
1,200
1,000
800
600
400
200
0
PRF of Avius (Hz)
0
200
400
600
800
1000
1200
1400
1600
PRF of LOGIQ E9 (Hz)
Joint
phantom
P1 LT-MCP2
P2 RT-MCP2
P2 RT-MCP3
P2 LT-MCP2
P2 LT-MCP3



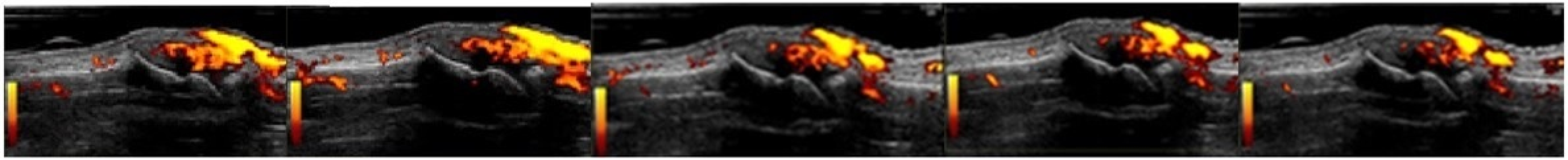
100
90
80
70
60
50
40
30
20
10
0
QPD index (%)
0
500
1000
1500
2000
PRF (Hz)
Joint
P1 LT-MCP2
P2 LT-MCP2
P2 RT-MCP3
P2 LT-MCP2
P2 LT-MCP3

Avius



PRF（Hz)	500	650	800	1000	1300
Grading score	3	3	2	2	2
QPDI	60.0	54.4	49.5	44.8	33.2

LOGIQ E9



PRF（Hz)	600	800	1000	1200	1500
Grading score	2	2	2	2	2
QPDI	38.2	34.2	29.0	26.7	19.0

PRF, pulse repetition frequency; QPD index, quantitative power Doppler index; MCP, metacarpophalangeal joint