



**HAL**  
open science

## Changes in blood flow velocity in the radial artery after 1-hour of ultrasound monitoring using a diagnostic 1 - 5 MHz transcranial probe – a pilot study

Petr Bardoň, David Školoudík, Kateřina Langová, Roman Herzig, Petr Kaňovský

### ► To cite this version:

Petr Bardoň, David Školoudík, Kateřina Langová, Roman Herzig, Petr Kaňovský. Changes in blood flow velocity in the radial artery after 1-hour of ultrasound monitoring using a diagnostic 1 - 5 MHz transcranial probe – a pilot study. *Journal of Clinical Ultrasound*, 2010, 38 (9), pp.493. 10.1002/jcu.20732 . hal-00572612

**HAL Id: hal-00572612**

**<https://hal.science/hal-00572612>**

Submitted on 2 Mar 2011

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



**Changes in blood flow velocity in the radial artery after 1-hour of ultrasound monitoring using a diagnostic 1 - 5 MHz transcranial probe – a pilot study**

Journal:	<i>Journal of Clinical Ultrasound</i>
Manuscript ID:	JCU-09-358.R1
Wiley - Manuscript type:	Research Article
Keywords:	ultrasound, blood flow oscillations, transcranial probe, sonothrombolysis



Review

1  
2  
3 **Changes in blood flow velocity in the radial artery after 1-hour of ultrasound**  
4  
5 **monitoring using a diagnostic 1 - 5 MHz transcranial probe – a pilot study**  
6  
7  
8  
9

10  
11  
12  
13  
14  
15 **Running head:** Doppler monitoring of radial artery  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

For Peer Review

**Abstract**

Purpose: Multiple biological effects of ultrasound on the human body have been described.

The aim was to monitor changes in blood flow velocities in the radial artery (RA) during continuous **pulsed wave** Doppler monitoring (DM).

Methods: Fifteen healthy volunteers (8 males; mean age  $54.7 \pm 17.0$  years) underwent 1-hour DM the left RA using a diagnostic transcranial 2-MHz probe. The measurements of blood flow velocities in 2-minute intervals were performed twice. During both sessions, the peak systolic velocity (PSV), end-diastolic velocity (EDV), mean flow velocity (MFV), pulsatile index (PI), and resistive index (RI) were recorded. During the first session, the recording was intermittent (monitoring period  $<10$  s). During the second session 2 weeks later, continual DM was performed.

Results: Irregular changes in the measured parameters were recorded during both sessions.

The changes in the blood flow parameters during the intermittent measurement were similar in positive and negative deflections. In contrast, an increase in EDV, and decreases in PI and RI were significantly higher during the continual DM ( $p=0.04$ ,  $p=0.04$ , and  $p=0.03$ , respectively). The changes in PSV and MFV did not differ between both measurements.

Conclusions: One-hour ultrasound Doppler monitoring using a 2-MHz diagnostic transcranial probe may lead to repetitive peripheral vasodilatation in humans.

Key words: ultrasound, blood flow oscillations, transcranial probe, sonothrombolysis

## Introduction

Multiple biological effects of ultrasound on the human body have been described. In the last 4 decades, different therapeutic effects of ultrasound have been studied experimentally. One such application involves accelerated recanalizing occluded arteries (clot lysis), especially in patients with acute strokes<sup>1-6</sup>. Various **intensities** (0.2 – 2.0 W/cm<sup>2</sup>) and frequencies (20 kHz – 2 MHz) of the ultrasound beam were used in previous studies<sup>1,4-7</sup>. There are two possible effects of the ultrasound beam on an occluded artery: 1) mechanical destruction due to thrombus vibration with acceleration of penetration of fibrinolytics into the thrombus, and 2) stimulation of the endothelium with activation of fibrinolysis<sup>1,7,8</sup>. Another possible effect of the ultrasound beam was observed during our previous study in which repeated marked vasodilatation of the peripheral artery during continual Doppler monitoring was recorded<sup>9</sup>.

The aims of this prospective pilot study were to confirm the effect of continual ultrasound monitoring in the **pulsed wave (PW)** Doppler mode using a standard diagnostic 1 - 5 MHz probe with a maximal diagnostic **intensity** (~~i.e., sono thrombolysis~~) on blood flow in human arteries.

## Materials and Methods

Fifteen volunteers were enrolled in the study during 6 months. All subjects fulfilled the inclusion and exclusion criteria, as listed in Table 1.

In all subjects, the measurement of blood flow velocities and indices in the radial artery (RA) were performed in 2-minute intervals during a 1-hour period in sessions A and B. The peak systolic velocity (PSV), end-diastolic velocity (EDV), mean flow velocity (MFV), pulsatile index (PI;  $PI = [PSV - EDV] / MFV$ ), and resistive index (RI;  $RI = [PSV - EDV] / EDV$ ) were obtained from a proximal part of the left RA as a mean value from last five heart cycles during both sessions. A sample volume (SV = 10 mm) was inserted in the proximal third of the RA to a depth of 15 - 35 mm, and the probe was held by hand in the same position during the entire session. During the session A, the probe was held in the same position during the whole session but the Doppler mode insonation with recording of blood flow velocities and indices was only intermittent. ~~In contrast to the session B~~ Thus in session A, the arterial segment was continuously insonated for a period < 10 seconds during each 2-minute interval. During the session B, the probe was also held in the same position during the whole session but continual ultrasound monitoring was performed in the Doppler mode (mechanical index [MI] = 1.4). Eight patients started with session A and 7 patients with session B. Time interval between both sessions was  $14 \pm 2$  days. A standard diagnostic duplex transcranial 1 – 5 MHz probe (P17; Aloka SSD 4000, Tokyo, Japan) was used during both sessions.

The maximum diagnostic thermal and mechanical indices of the ultrasound beam (mechanical index (MI) = 1.4, tissue thermal index (Tlc) = 1.9) was set in Doppler mode. The pulsed wave (PW) Doppler mode with frequency of ultrasound beam 2.0 MHz was used. Insonation depth was between 15 and 35 mm with sample volume 10 mm. The following sonographic machine setting was used: pulse repetition period 0.2 ms, burst repetition

1  
2  
3 frequency 5000 Hz, pulse duration 1.46  $\mu$ s, peak rarefactional pressure 2.24 MPa, and pulse  
4  
5 average intensity at maximum MI 208 W/cm<sup>2</sup>.  
6  
7

8 All measurements were performed in a quiet room with a constant temperature.  
9  
10 Patients were lying in a comfortable position. The measurement started before noon, 4 – 6  
11  
12 hours after the last meal, and minimally 24 hours after the last consumption of alcohol or  
13  
14 caffeine.  
15  
16

17 Physical examinations were performed before the beginning of the session, at the end  
18  
19 of the session, 24 hours after each session, and 30 days after the second session; all adverse  
20  
21 events were recorded. All changes in physical examinations and all disorders requiring  
22  
23 hospitalization were recorded as an adverse event.  
24  
25  
26  
27  
28

#### 29 *Ethics committee approval*

30  
31 The local Ethics Committee at the University Hospital Ostrava approved the study and  
32  
33 at the time of enrollment, each volunteer signed an informed consent form. The entire study  
34  
35 was conducted in accordance with the Helsinki Declaration of 1975, as revised in 1983 and  
36  
37 2008.  
38  
39  
40  
41  
42

#### 43 *Statistical analysis*

44  
45 Data are reported as the median  $\pm$  standard deviation with a coefficient of variation.  
46  
47 The one-sample Student's t-test was applied when assessing statistical significance of the  
48  
49 differences between the PSV, EDV, MFV, PI, and RI during both sessions. Statistical  
50  
51 evaluations were performed using SPSS, version 15.0 (SPSS, Inc., Chicago, IL, USA).  
52  
53  
54  
55 Statistical significance was defined as a  $p$  value  $< 0.05$ .  
56  
57  
58  
59  
60

## Results

The sample of healthy volunteers consisted of 8 males and 7 females, with ages ranging between 30 and 78 years, and a mean age of  $54.7 \pm 17.0$  years. Irregular changes in the measured parameters were recorded during both sessions. The changes in the blood flow parameters during the session A with intermittent measurement were similar in positive and negative deflections (Table 2). In contrast, the increase in EDV, and decrease in PI and RI were significantly higher during the session B with continual Doppler monitoring ( $p = 0.004$ ,  $p = 0.004$ , and  $p = 0.015$ , respectively) with higher coefficients of variation. Several episodes of transient vasodilatation were observed during 1-hour monitoring in this session. The changes in PSV and MFV did not significantly differ between both measurements (Table 2).

The mean change in blood pressure during the first and second sessions was  $6.1 \pm 6.3$  and  $6.7 \pm 7.1$  mm Hg, respectively. The difference was not statistically significant. No clinically adverse events were recorded during and after the Doppler monitoring of the RA.

## Discussion

This is the first study in which the changes in blood flow velocity and indices during intermittent and continual Doppler monitoring (~~sono-thrombolysis~~) were compared.

The results of the presented study demonstrated that 60-minutes of Doppler monitoring using a 1 - 5 MHz diagnostic duplex transcranial probe with maximal intensity may directly affect peripheral resistance (arterial tonus) in the territory of the monitored artery. However, the magnitude of the changes observed was not clinically significant in intact radial artery.

We hypothesize that Doppler monitoring of a peripheral artery in the human body may lead to irritation of the endothelium. This mechanical irritation with a probable local increase in temperature may stimulate nitride oxide (NO) synthesis and secretion with peripheral vasodilatation, characterized by the EDV increase and the decrease of peripheral resistance (as assessed using the PI and RI). The variation in peripheral resistance could be explained by the short half-time of NO with new re-synthesis<sup>10</sup>. Also, prostaglandin-2 and aspartate could play a role in this peripheral vasodilatation<sup>11</sup>.

One can take exception to the possibility of an increase of EDV due to variable pressure on the monitored artery caused by the ultrasound probe. However, increased pressure on the artery usually leads to an increase in the PSV and sometimes a decrease in the EDV with an increase in PI and RI. We did not record this situation in our study.

The effect of TCD monitoring on thrombus dissolution in acute stroke patients was demonstrated for the first time in 2000<sup>12</sup>. Subsequently, other studies demonstrated a potential effect of diagnostic ultrasound on the acceleration of spontaneous or induced recanalization of intracranial arteries with better clinical outcome after 90 days<sup>4-6</sup>. This therapeutic procedure is referred to as sono-thrombolysis.

## Doppler monitoring of radial artery 8

1  
2  
3 The results of the presented pilot study showed that in addition to the two possible  
4 effects of an ultrasound beam (mechanical thrombus destruction with penetration of  
5 fibrinolytics into the thrombus and activation of the endogenous fibrinolytic system)<sup>1,7,8</sup>, there  
6 should be another effect causing acceleration of artery recanalization and improvement of  
7 blood flow in the territory of the occluded artery (intermittent distal vasodilatation in the  
8 territory of a monitored artery).  
9  
10  
11  
12  
13  
14  
15  
16

17 Some limitations of the current study should be mentioned. The study set was  
18 relatively small and the influence of risk factors (e.g., hypertension, diabetes mellitus, and  
19 atherosclerosis) could not be evaluated. In addition, the factors influencing blood flow, e.g.,  
20 arterial blood pressure, blood oxygen saturation, and partial pressure of CO<sub>2</sub> and O<sub>2</sub>, were not  
21 continually monitored. It is also known that flow to the hand is highly variable and is  
22 governed by sympathetic neural inputs, temperature, and stress. Nevertheless, we only  
23 compared the changes of the measured blood flow parameters between two sessions in the  
24 same subject in which we presumed a similar variation of these factors and, the influence of  
25 stress was similar during both sessions, as the subjects had to remain still for an hour and  
26 were not aware of the type of sonographic insonation (intermittent versus continual) in both  
27 cases. For elimination of these limitations, a new study with continual measurement of all the  
28 mentioned factors will be initiated.  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

## Conclusion

A 1-hour continuous Doppler monitoring of RA using transcranial 1 – 5 MHz duplex probe may directly lead to the repetitive peripheral vasodilatation without causing any clinically relevant adverse effects. Further studies are needed for a complete explanation of the effect of various ultrasound frequencies and **intensities** on the human arterial system.

For Peer Review

**References**

1. Daffertshofer M, Fatar M. Therapeutic ultrasound in ischemic stroke treatment: experimental evidence. *Eur J Ultrasound* 2002;16:121-130.
2. Francis CW, Onundarson PT, Carstensen EL, et al. Enhancement of fibrinolysis in vitro by ultrasound. *J Clin Invest* 1992;90:2063-2068.
3. Ishibashi T, Akiyama M, Onoue H, et al. Can transcranial ultrasonication increase recanalization flow with tissue plasminogen activator? *Stroke* 2002;33:1399-1404.
4. Alexandrov AV, Demchuk AM, Burgin WS, et al.; CLOTBUST Investigators. Ultrasound-enhanced thrombolysis for acute ischemic stroke: phase I. Findings of the CLOTBUST trial. *J Neuroimaging* 2004;14:113-117.
5. Eggers J, Seidel G, Koch B, et al. Sonothrombolysis in acute ischemic stroke for patients ineligible for rt-PA. *Neurology* 2005;64:1052-1054.
6. Školoudík D, Bar M, Škoda O, et al. Safety and Efficacy of the Sonographic Acceleration of the Middle Cerebral Artery Recanalization: Results of the pilot Thrombotripsy Study. *Ultrasound Med Biol* 2008;34:1775-1782.
7. Francis CW, Behrens S. Ultrasonic thrombolysis. In: Hennerici M, Meairs S, editors. *Cerebrovascular ultrasound*. Cambridge, UK: University Press; 2001: pp 404-415.
8. Školoudík D, Fadrná T, Bar M, et al. Changes in haemocoagulation in healthy volunteers after a 1-hour thrombotripsy using a diagnostic 2-4 MHz transcranial probe. *J Tromb Tromb* 2008;26:119-124.
9. Školoudík D, Bar M, Blatný J, et al. Biological effect of thrombotripsy – 1-hour TCD monitoring using a diagnostic 2-4 MHz transcranial probe. [abstract] *Cerebrovasc Dis* 2008;26(Suppl 1):6.

- 1  
2  
3 10. Chatterjee A, Catravas JD. Endothelial nitric oxide (NO) and its pathophysiologic  
4 regulation. *Vascul Pharmacol* 2008;49:134-140.  
5  
6  
7  
8 11. Aird WC. Endothelium as an organ system. *Crit Care Med* 2004;32(Suppl 5):S271-279.  
9  
10 12. Alexandrov AV, Demchuk AM, Felberg RA, et al. High rate of complete recanalisation  
11 and dramatic clinical recovery during tPA infusion when continuously monitored with 2-MHz  
12 transcranial Doppler monitoring. *Stroke* 2000;31:610-614.  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

For Peer Review

**Tables**

Table 1. Study inclusion and exclusion criteria.

Table 2. Mean baseline values, coefficients of variation and mean changes in peak systolic velocity, end-diastolic velocity, mean flow velocity, pulsatility index and resistive index during intermittent Doppler measurement (session A) and continual Doppler monitoring (session B) of the radial artery.

1  
2  
3 **Changes in blood flow velocity in the radial artery after 1-hour of ultrasound**  
4  
5 **monitoring using a diagnostic 1 - 5 MHz transcranial probe – a pilot study**  
6  
7  
8  
9

10  
11  
12  
13  
14  
15 **Running head:** Doppler monitoring of radial artery  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

For Peer Review

**Abstract**

Purpose: Multiple biological effects of ultrasound on the human body have been described.

The aim was to monitor changes in blood flow velocities in the radial artery (RA) during continuous pulsed wave Doppler monitoring (DM).

Methods: Fifteen healthy volunteers (8 males; mean age  $54.7 \pm 17.0$  years) underwent 1-hour DM the left RA using a diagnostic transcranial 2-MHz probe. The measurements of blood flow velocities in 2-minute intervals were performed twice. During both sessions, the peak systolic velocity (PSV), end-diastolic velocity (EDV), mean flow velocity (MFV), pulsatile index (PI), and resistive index (RI) were recorded. During the first session, the recording was intermittent (monitoring period  $<10$  s). During the second session 2 weeks later, continual DM was performed.

Results: Irregular changes in the measured parameters were recorded during both sessions.

The changes in the blood flow parameters during the intermittent measurement were similar in positive and negative deflections. In contrast, an increase in EDV, and decreases in PI and RI were significantly higher during the continual DM ( $p=0.04$ ,  $p=0.04$ , and  $p=0.03$ , respectively). The changes in PSV and MFV did not differ between both measurements.

Conclusions: One-hour ultrasound Doppler monitoring using a 2-MHz diagnostic transcranial probe may lead to repetitive peripheral vasodilatation in humans.

Key words: ultrasound, blood flow oscillations, transcranial probe, sonothrombolysis

## Introduction

Multiple biological effects of ultrasound on the human body have been described. In the last 4 decades, different therapeutic effects of ultrasound have been studied experimentally. One such application involves accelerated recanalizing occluded arteries (clot lysis), especially in patients with acute strokes<sup>1-6</sup>. Various intensities (0.2 – 2.0 W/cm<sup>2</sup>) and frequencies (20 kHz – 2 MHz) of the ultrasound beam were used in previous studies<sup>1,4-7</sup>. There are two possible effects of the ultrasound beam on an occluded artery: 1) mechanical destruction due to thrombus vibration with acceleration of penetration of fibrinolytics into the thrombus, and 2) stimulation of the endothelium with activation of fibrinolysis<sup>1,7,8</sup>. Another possible effect of the ultrasound beam was observed during our previous study in which repeated marked vasodilatation of the peripheral artery during continual Doppler monitoring was recorded<sup>9</sup>.

The aims of this prospective pilot study were to confirm the effect of continual ultrasound monitoring in the pulsed wave (PW) Doppler mode using a standard diagnostic 1 - 5 MHz probe with a maximal diagnostic intensity on blood flow in human arteries.

## Materials and Methods

Fifteen volunteers were enrolled in the study during 6 months. All subjects fulfilled the inclusion and exclusion criteria, as listed in Table 1.

In all subjects, the measurement of blood flow velocities and indices in the radial artery (RA) were performed in 2-minute intervals during a 1-hour period in sessions A and B. The peak systolic velocity (PSV), end-diastolic velocity (EDV), mean flow velocity (MFV), pulsatile index (PI;  $PI = [PSV - EDV] / MFV$ ), and resistive index (RI;  $RI = [PSV - EDV] / EDV$ ) were obtained from a proximal part of the left RA as a mean value from last five heart cycles during both sessions. A sample volume (SV = 10 mm) was inserted in the proximal third of the RA to a depth of 15 - 35 mm, and the probe was held by hand in the same position during the entire session. During the session A, the probe was held in the same position during the whole session but the Doppler mode insonation with recording of blood flow velocities and indices was only intermittent. Thus in session A, the arterial segment was continuously insonated for a period < 10 seconds during each 2-minute interval. During session B, the probe was also held in the same position during the whole session but continual ultrasound monitoring was performed in the Doppler mode (mechanical index [MI] = 1.4). Eight patients started with session A and 7 patients with session B. Time interval between both sessions was  $14 \pm 2$  days. A standard diagnostic duplex transcranial 1 – 5 MHz probe (P17; Aloka SSD 4000, Tokyo, Japan) was used during both sessions.

The maximum diagnostic thermal and mechanical indices of the ultrasound beam (mechanical index (MI) = 1.4, tissue thermal index (TI<sub>c</sub>) = 1.9) was set in Doppler mode. The pulsed wave (PW) Doppler mode with frequency of ultrasound beam 2.0 MHz was used. Insonation depth was between 15 and 35 mm with sample volume 10 mm. The following sonographic machine setting was used: pulse repetition period 0.2 ms, burst repetition

1  
2  
3 frequency 5000 Hz, pulse duration 1.46  $\mu$ s, peak rarefactional pressure 2.24 MPa, and pulse  
4  
5 average intensity at maximum MI 208 W/cm<sup>2</sup>.  
6  
7

8 All measurements were performed in a quiet room with a constant temperature.  
9  
10 Patients were lying in a comfortable position. The measurement started before noon, 4 – 6  
11  
12 hours after the last meal, and minimally 24 hours after the last consumption of alcohol or  
13  
14 caffeine.  
15  
16

17 Physical examinations were performed before the beginning of the session, at the end  
18  
19 of the session, 24 hours after each session, and 30 days after the second session; all adverse  
20  
21 events were recorded. All changes in physical examinations and all disorders requiring  
22  
23 hospitalization were recorded as an adverse event.  
24  
25  
26  
27  
28  
29

### 30 *Ethics committee approval*

31  
32  
33 The local Ethics Committee at the University Hospital Ostrava approved the study and  
34  
35 at the time of enrollment, each volunteer signed an informed consent form. The entire study  
36  
37 was conducted in accordance with the Helsinki Declaration of 1975, as revised in 1983 and  
38  
39 2008.  
40  
41  
42  
43

### 44 *Statistical analysis*

45  
46  
47 Data are reported as the median  $\pm$  standard deviation with a coefficient of variation.  
48  
49 The one-sample Student's t-test was applied when assessing statistical significance of the  
50  
51 differences between the PSV, EDV, MFV, PI, and RI during both sessions. Statistical  
52  
53 evaluations were performed using SPSS, version 15.0 (SPSS, Inc., Chicago, IL, USA).  
54  
55  
56 Statistical significance was defined as a  $p$  value  $< 0.05$ .  
57  
58  
59  
60

## Results

The sample of healthy volunteers consisted of 8 males and 7 females, with ages ranging between 30 and 78 years, and a mean age of  $54.7 \pm 17.0$  years. Irregular changes in the measured parameters were recorded during both sessions. The changes in the blood flow parameters during the session A with intermittent measurement were similar in positive and negative deflections (Table 2). In contrast, the increase in EDV, and decrease in PI and RI were significantly higher during the session B with continual Doppler monitoring ( $p = 0.004$ ,  $p = 0.004$ , and  $p = 0.015$ , respectively) with higher coefficients of variation. Several episodes of transient vasodilatation were observed during 1-hour monitoring in this session. The changes in PSV and MFV did not significantly differ between both measurements (Table 2).

The mean change in blood pressure during the first and second sessions was  $6.1 \pm 6.3$  and  $6.7 \pm 7.1$  mm Hg, respectively. The difference was not statistically significant. No clinically adverse events were recorded during and after the Doppler monitoring of the RA.

## Discussion

This is the first study in which the changes in blood flow velocity and indices during intermittent and continual Doppler monitoring were compared.

The results of the presented study demonstrated that 60-minutes of Doppler monitoring using a 1 - 5 MHz diagnostic duplex transcranial probe with maximal intensity may directly affect peripheral resistance (arterial tonus) in the territory of the monitored artery. However, the magnitude of the changes observed was not clinically significant in intact radial artery.

We hypothesize that Doppler monitoring of a peripheral artery in the human body may lead to irritation of the endothelium. This mechanical irritation with a probable local increase in temperature may stimulate nitric oxide (NO) synthesis and secretion with peripheral vasodilatation, characterized by the EDV increase and the decrease of peripheral resistance (as assessed using the PI and RI). The variation in peripheral resistance could be explained by the short half-time of NO with new re-synthesis<sup>10</sup>. Also, prostaglandin-2 and aspartate could play a role in this peripheral vasodilatation<sup>11</sup>.

One can take exception to the possibility of an increase of EDV due to variable pressure on the monitored artery caused by the ultrasound probe. However, increased pressure on the artery usually leads to an increase in the PSV and sometimes a decrease in the EDV with an increase in PI and RI. We did not record this situation in our study.

The effect of TCD monitoring on thrombus dissolution in acute stroke patients was demonstrated for the first time in 2000<sup>12</sup>. Subsequently, other studies demonstrated a potential effect of diagnostic ultrasound on the acceleration of spontaneous or induced recanalization of intracranial arteries with better clinical outcome after 90 days<sup>4-6</sup>. This therapeutic procedure is referred to as sono-thrombolysis.

## Doppler monitoring of radial artery 8

1  
2  
3 The results of the presented pilot study showed that in addition to the two possible  
4 effects of an ultrasound beam (mechanical thrombus destruction with penetration of  
5 fibrinolytics into the thrombus and activation of the endogenous fibrinolytic system)<sup>1,7,8</sup>, there  
6 should be another effect causing acceleration of artery recanalization and improvement of  
7 blood flow in the territory of the occluded artery (intermittent distal vasodilatation in the  
8 territory of a monitored artery).  
9  
10  
11  
12  
13  
14  
15  
16

17 Some limitations of the current study should be mentioned. The study set was  
18 relatively small and the influence of risk factors (e.g., hypertension, diabetes mellitus, and  
19 atherosclerosis) could not be evaluated. In addition, the factors influencing blood flow, e.g.,  
20 arterial blood pressure, blood oxygen saturation, and partial pressure of CO<sub>2</sub> and O<sub>2</sub>, were not  
21 continually monitored. It is also known that flow to the hand is highly variable and is  
22 governed by sympathetic neural inputs, temperature, and stress. Nevertheless, we only  
23 compared the changes of the measured blood flow parameters between two sessions in the  
24 same subject in which we presumed a similar variation of these factors and, the influence of  
25 stress was similar during both sessions, as the subjects had to remain still for an hour and  
26 were not aware of the type of sonographic insonation (intermittent versus continual) in both  
27 cases. For elimination of these limitations, a new study with continual measurement of all the  
28 mentioned factors will be initiated.  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

**Conclusion**

A 1-hour continuous Doppler monitoring of RA using transcranial 1 – 5 MHz duplex probe may directly lead to the repetitive peripheral vasodilatation without causing any clinically relevant adverse effects. Further studies are needed for a complete explanation of the effect of various ultrasound frequencies and intensities on the human arterial system.

For Peer Review

**References**

1. Daffertshofer M, Fatar M. Therapeutic ultrasound in ischemic stroke treatment: experimental evidence. *Eur J Ultrasound* 2002;16:121-130.
2. Francis CW, Onundarson PT, Carstensen EL, et al. Enhancement of fibrinolysis in vitro by ultrasound. *J Clin Invest* 1992;90:2063-2068.
3. Ishibashi T, Akiyama M, Onoue H, et al. Can transcranial ultrasonication increase recanalization flow with tissue plasminogen activator? *Stroke* 2002;33:1399-1404.
4. Alexandrov AV, Demchuk AM, Burgin WS, et al.; CLOTBUST Investigators. Ultrasound-enhanced thrombolysis for acute ischemic stroke: phase I. Findings of the CLOTBUST trial. *J Neuroimaging* 2004;14:113-117.
5. Eggers J, Seidel G, Koch B, et al. Sonothrombolysis in acute ischemic stroke for patients ineligible for rt-PA. *Neurology* 2005;64:1052-1054.
6. Školoudík D, Bar M, Škoda O, et al. Safety and Efficacy of the Sonographic Acceleration of the Middle Cerebral Artery Recanalization: Results of the pilot Thrombotripsy Study. *Ultrasound Med Biol* 2008;34:1775-1782.
7. Francis CW, Behrens S. Ultrasonic thrombolysis. In: Hennerici M, Meairs S, editors. *Cerebrovascular ultrasound*. Cambridge, UK: University Press; 2001: pp 404-415.
8. Školoudík D, Fadrná T, Bar M, et al. Changes in haemocoagulation in healthy volunteers after a 1-hour thrombotripsy using a diagnostic 2-4 MHz transcranial probe. *J Tromb Tromb* 2008;26:119-124.
9. Školoudík D, Bar M, Blatný J, et al. Biological effect of thrombotripsy – 1-hour TCD monitoring using a diagnostic 2-4 MHz transcranial probe. [abstract] *Cerebrovasc Dis* 2008;26(Suppl 1):6.

10. Chatterjee A, Catravas JD. Endothelial nitric oxide (NO) and its pathophysiologic regulation. *Vascul Pharmacol* 2008;49:134-140.
11. Aird WC. Endothelium as an organ system. *Crit Care Med* 2004;32(Suppl 5):S271-279.
12. Alexandrov AV, Demchuk AM, Felberg RA, et al. High rate of complete recanalisation and dramatic clinical recovery during tPA infusion when continuously monitored with 2-MHz transcranial Doppler monitoring. *Stroke* 2000;31:610-614.

For Peer Review

**Tables**

Table 1. Study inclusion and exclusion criteria.

Table 2. Mean baseline values, coefficients of variation and mean changes in peak systolic velocity, end-diastolic velocity, mean flow velocity, pulsatility index and resistive index during intermittent Doppler measurement (session A) and continual Doppler monitoring (session B) of the radial artery.

Table 1. Study inclusion and exclusion criteria.

	Age 30 - 80 years
<u>Inclusion criteria</u>	Informed consent signed
	Known nephropathy with creatinine level > 150 µmol/L or creatinine clearance < 30 ml per hour
	Hepatopathy with elevation of hepatic enzymes or bilirubin > 2 times the upper limit of normal
<u>Exclusion criteria</u>	Planned therapy using fibrinolytics or high dose heparin during 24 hours after the enrolment into the study
	peripheral artery disease
	History of vascular surgery

Table 2. Mean baseline values, coefficients of variation and mean changes in peak systolic velocity, end-diastolic velocity, mean flow velocity, pulsatile index and resistive index during intermittent Doppler measurement (session A) and continual Doppler monitoring (session B) of the radial artery

	Mean baseline value $\pm$ SD		p value	coefficient of variation		Mean change $\pm$ SD		p value	Mean difference	95% confidence interval of the difference
	IDM	CDM		IDM	CDM	IDM	CDM			
<b>PSV (cm/s)</b>	59.07 $\pm$ 10.40	58.53 $\pm$ 10.06	0.155	18.8%	18.6%	-0.61 $\pm$ 8.03	-0.75 $\pm$ 8.79	0.814	-0.138	-1.372 – 1.097
<b>EDV (cm/s)</b>	10.47 $\pm$ 2.87	10.33 $\pm$ 2.98	0.217	29.2%	37.3%	-0.41 $\pm$ 2.33	0.54 $\pm$ 3.59	<b>0.004</b>	0.948	0.348 – 1.549
<b>MFV (cm/s)</b>	26.75 $\pm$ 4.94	26.41 $\pm$ 4.98	0.120	19.0%	18.8%	-0.56 $\pm$ 3.76	0.07 $\pm$ 4.65	0.086	0.629	-0.102 – 1.361
<b>PI</b>	1.831 $\pm$ 0.177	1.843 $\pm$ 0.180	0.287	12.7%	18.3%	0.020 $\pm$ 0.201	-0.043 $\pm$ 0.289	<b>0.004</b>	-0.017	-0.029 – -0.006
<b>RI</b>	0.819 $\pm$ 0.038	0.821 $\pm$ 0.036	0.304	5.5%	9.8%	0.004 $\pm$ 0.035	-0.013 $\pm$ 0.059	<b>0.015</b>	-0.018	-0.031 – -0.004

CDM – continual Doppler monitoring (session B), EDV – end-diastolic velocity, IDM – intermittent Doppler measurement (session A), MFV – mean flow velocity, PI – pulsatility index, PSV – peak systolic velocity, RI – resistive index, SD – standard deviation