Med Bio Eng Comput (2006) 44:501–509
DOI 10.1007/s11517-006-0070-0

ORIGINAL ARTICLE

Non-invasive continuous estimation of blood flow changes in human patellar bone

Jan Näslund · Jonas Pettersson · Thomas Lundeberg · Dag Linnarsson · Lars-Göran Lindberg

Received: 27 March 2006 / Accepted: 4 May 2006 / Published online: 3 June 2006
© International Federation for Medical and Biological Engineering 2006

Abstract A photoplethysmographic (PPG) technique to assess blood flow in bone tissue has been developed and tested. The signal detected by the PPG consists of a constant-level (DC) component—which is related to the relative vascularization of the tissue—and a pulsatile (AC) component—which is synchronous with the pumping action of the heart. The PPG probe was applied on the skin over the patella. The probe uses near-infrared (804 nm) and green (560 nm) light sources and the AC component of the PPG signals of the two wavelengths was used to monitor pulsatile blood flow in the patellar bone and the overlying skin, respectively. Twenty healthy subjects were studied and arterial occlusion resulted in elimination of PPG signals at both wavelengths, whereas occlusion of skin blood flow by local surface pressure eliminated only the PPG signal at 560 nm. In a parallel study on a physical model with a rigid tube we showed that the AC component of the PPG signal originates from pulsations of blood flow in a rigid structure and not necessarily from volume pulsations. We conclude that pulsatile blood flow in the patellar bone can be assessed with the present PPG technique.

J. Näslund (✉) · D. Linnarsson
Department of Physiology and Pharmacology,
Karolinska Institutet, 171 77 Stockholm, Sweden
e-mail: j.naslund@mailbox.calypso.net

J. Pettersson · L.-G. Lindberg
Department of Biomedical Engineering,
Linköping University, Linkoping, Sweden

T. Lundeberg
Rehabilitation Medicine University Clinic Stockholm,
Danderyds Hospital, Stockholm, Sweden

Keywords Bone · Perfusion · Pulsatile · Photoplethysmography · Near-infrared light

1 Introduction

1.1 Clinical and anatomical background

Knowledge of regional organ perfusion plays a key role in understanding the physiologic and pathophysiologic processes in various organs. Determinations of actual skeletal blood flow are not easily made in humans [21]. Different methods measure different levels of the circulatory system, such as limb blood flow and local microcirculation. Blood flow in bone tissue has been evaluated using bone scintigraphy [8], single-photon emission computed tomography [11], Doppler ultrasonography [21], radionuclide-labeled and fluorescent microspheres [1], positron emission tomography [15], laser-Doppler flowmetry [14, 25], and intravital microscopy television system in combination with confocal laser-scanning optics [20]. The last two techniques require surgical manipulation of the bone and therefore may introduce artifacts attributable to local manipulation of the vessels. Near-infrared spectroscopy has been used to assess the perfusion index in the tibia bone marrow [3]. To our knowledge no method for measuring local blood flow in human bone tissue continuously and non-invasively has been previously published.

Photoplethysmography (PPG) is a non-invasive optical technique for assessing blood flow-related phenomena. Although it has mainly been used to assess blood perfusion in skin [16], it has also been used for measuring muscle blood flow [30, 33]. Recently, the

technique has been used to study the effects of sensory stimulation on blood flow in muscle tissue [29].

In the present study, blood flow was studied in the patella during different types of interventions. Anterior to the patella and deep to the skin is a trilaminar arrangement of fibrous soft tissue. These structures include a transversely oriented fascia, an obliquely oriented aponeurosis, and the longitudinally oriented fibers of the rectus femoris tendon [9]. The patellar bone is made up of a thin, superficial layer of cortical bone that covers a center of trabecular bone. The patella has no bone marrow cavity, granting that the sample volume mainly consists of trabecular bone [14].

The patella has extraosseous (Fig. 1) and intraosseous arterial patterns (Fig. 2). The extraosseous arteries comprise an anastomotic ring composed of the supreme genicular, medial superior genicular, medial inferior genicular, lateral superior genicular, and lateral inferior genicular arteries and the anterior tibial recurrent artery [31]. The intraosseous arteries are grouped into two main systems. The first comprises the midpatellar vessels, which enter 10–12 vascular forminae located on the middle third of the anterior surface in an oblique direction from inferior to superior. Bonutti et al. [4] stated that the main supply of arterial blood to the patella flows through this system. The second system arises from the polar vessels through the deep inferior patellar surface upward, supplying the lowermost one-third of the patella and communicating within the bone with branches of the midpatellar vessels [11].

It has been shown that all perfusion in the patella originates from arteries identified as descending from the poplitea artery proximal to the femur condyles (Fig. 1) [4]. Intraosseous phlebography of the patella indicates that the posterior surface of the apex patellae is the most important exit for veins that drain this bone [2].

1.2 Theoretical basis of photoplethysmography

The PPG technique in reflection mode requires a light source and a photodetector (PD) placed adjacent to each other. The beam of light is directed toward the part of tissue in which blood flow is to be measured. The emitted light is reflected, absorbed, and scattered within the tissue, and only a small fraction of the emitted light is received by the PD. The intensity of the reflected and scattered light is recorded by the PD and assumed to be related to blood flow changes occurring underneath the probe [18]. The depth that light penetrates a tissue is primarily a function of wavelength and the optical geometry of the probe but also of the optical qualities of the tissues of interest.

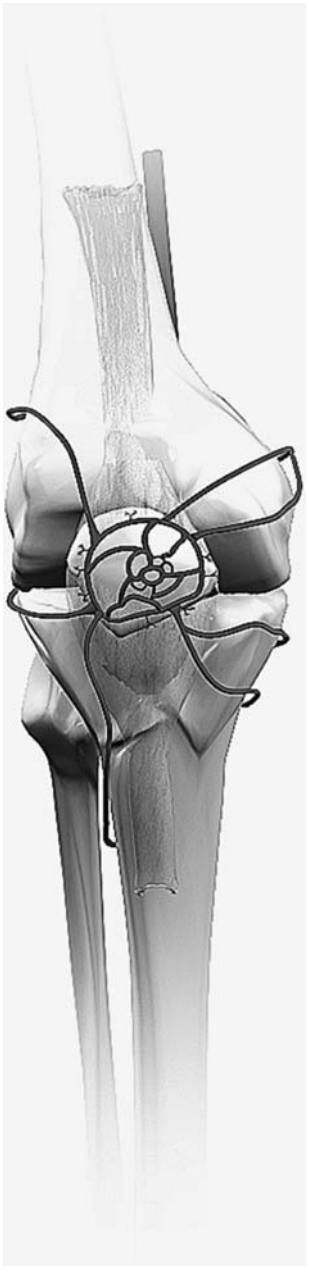

Fig. 1 Extraosseous arterial supply to the patella

The signal detected by the PPG consists of a constant-level (DC) component—which is related to the relative vascularization of the tissue—and a pulsatile (AC) component—which is synchronous with the pumping action of the heart. The amplitude of the heart-synchronous AC component is thought to be correlated to the blood flow under the probe [16].

It has mostly been suggested that the AC component is related to pulsatile volume changes due to varying lumen of the vessel [6, 16, 23, 24]. However, recordings from rigid tissues have shown

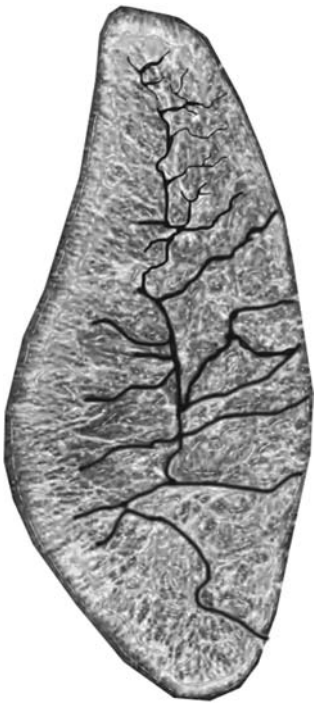

Fig. 2 Intraosseous arterial supply shown in a sagittal section. The anterior side is on the *right*. The scale is approximately ten times larger than in Fig. 1

pulse-synchronous PPG signals [28], and the pulsatile component of PPG recordings of the dental pulp has been used to detect blood flow and viability in teeth [22]. Moreover, it has been demonstrated in in vitro models that light transmission and reflection in blood can change with the velocity even if the volume of the illuminated blood is constant [19]. Therefore, it has been postulated that both the AC and the DC components in PPG depend on red blood cell (RBC) orientation, deformation, and axial migration [12, 19, 27, 28]. Such changes of RBC orientation are known to occur as a function of flow and shear rate [10].

1.3 Aims of the study

Our principal aim was to develop a method to study blood flow in bone tissue such as the patella. Therefore a PPG probe was designed and tested on healthy subjects during interventions leading to changes in tissue blood flow. Moreover, we addressed the issue whether changes in blood flow could give a rise to an AC component in the PPG signal in a rigid blood conduit, such as the vascular system in trabecular bone. For that purpose a physical model was investigated using light of a similar wavelength as in the human studies.

2 Methods

2.1 Photoplethysmography instrumentation for human measurements

The technique used in this study is based on specific assumptions described in Fig. 3, which schematically illustrates the photon distribution in the patella. The infrared light penetrates the skin as well as part of the bone, whereas the green light mainly is distributed in the skin before the total light arrives at the PD. A two-channel PPG instrument (Department of Biomedical Engineering, Linköping University, Linköping, Sweden) and a PPG probe were used to continuously record blood flow changes in the skin and the patellar bone. This newly designed probe for measurements of the patella (Figs. 4, 5) contains one near-infrared light-emitting diode (LED) at 804 nm for deep tissue, two green-light LEDs at 560 nm for monitoring blood flow at a depth of ~2 mm (skin), and one PD. All optical components were embedded in black-colored silicon (Fig. 4). The distance between the near-infrared LED

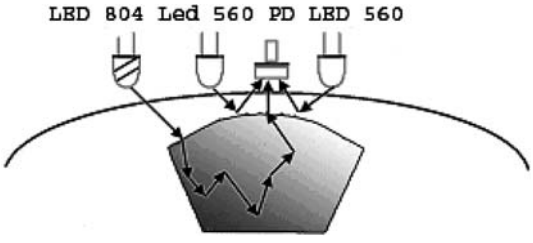

Fig. 3 Schematic representation of photon distribution during photoplethysmographic measurements on the patella. The *dark section* represents patellar bone, and the *white area* is soft tissue. *PD* photodetector, *LED* light-emitting diodes for the wavelengths 804 and 560 nm

Fig. 4 A PPG probe shown from below including three light-emitting diodes (*LEDs*) and a photodetector (*PD*). The dimensions of the probe are 50 mm×38 mm

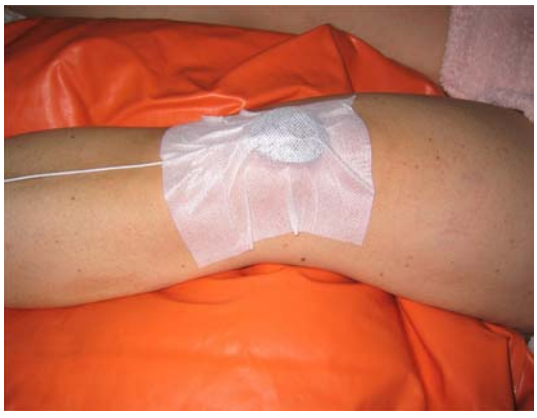

Fig. 5 PPG probe placed on the patella with adhesive tape

and the PD was 25 mm, and the distance between the green LEDs and the PD was 3.5 mm (Fig. 4).

The pulse-by-pulse amplitude of the AC component of the PPG signal at each wavelength was subsequently extracted with a dedicated software (Daquhura 1.3, Linköpings Tekniska Högskola 1995). Mean amplitudes were computed from series of 20 consecutive pulsations before (baseline), during, and after the interventions. The PD current was amplified in a current-to-voltage converter to establish the PPG signal and was further amplified using a programmable amplifier. After the DC amplifier the DC-portion of the signal was cut off using a passive RC-filter and the remaining AC-signal was amplified using a second programmable amplifier. The signals from each wavelength were adjusted to the same magnitude and stored on a personal computer.

2.2 Subjects

Twenty healthy normotensive subjects with no history of knee pain were recruited to participate in this study. All subjects, members of a health club, were used to physical activity. All PPG recordings were made on one occasion, and all subjects gave their informed consent to participate. The research ethics committee at the Faculty of Medicine, University of Lund, approved the study (Table 1).

Table 1 Anthropometric data of the subjects (mean, SD)

	Total	Female	Male
Subjects (*n*)	20	8	12
Age (years)	38 (9)	34 (9)	41 (9)
Height (cm)	176 (11)	163 (5)	185 (4)
Weight (kg)	78 (17)	62 (9)	89 (11)
Body mass index	25 (3)	23 (3)	26 (4)

2.3 Procedures in human measurements

The subjects lay in a supine position in a quiet room with moderate light and a room temperature of 23°C (±1°C). The PPG probe (newly designed for this study, Fig. 4) was placed over the center of the patellar bone and attached to the skin with adhesive tape (Fig. 5). A green-color cover was used to minimize the influence of ambient light during all measurements. After 15 min of rest, blood flow was recorded continuously from 60 s prior the intervention to 5 min after. Blood flow was measured with the knee fixed (by means of a vacuum pillow, AB Germa, Kristianstad, Sweden) in a position at 20° of flexion during all interventions (Fig. 5). One measurement was made on each knee. All interventions and measurements were made by one of the authors (J.N.). The PPG signal was analyzed by another author (L.-G.L.) who was blind to subject identity and recording conditions.

Various procedures were used to influence the blood flow superficially in the skin or in the patellar bone. The nature and purpose of the interventions are described in more detail below.

2.3.1 Vascular occlusion of skin tissue

After the initial 60 s of measurement to establish a reference value, a pressure of 100 mmHg was applied to the probe with an algometer (Somedic®, Stockholm, Sweden) to occlude the skin blood flow. The pressure was applied for 60 s, after which the pressure was removed. The purpose of this experiment was to investigate the ability of the PPG instrument to differentiate between skin and bone blood flow when the blood flow in the skin was occluded.

2.3.2 Venous occlusion

After the initial 60 s of measurement to establish a reference value, a pressure of 60 mmHg was applied around the thigh with a blood-pressure cuff to decrease the venous blood flow [13]. The cuff remained inflated for 60 s, after which the pressure was released. The purpose of this experiment was to investigate how the PPG signal responds to partially decreased blood flow in tissue segments upstream to venous occlusion.

2.3.3 Arterial occlusion

After the initial 60 s of measurement to establish a reference value, a pressure of 180 mmHg was applied around the thigh with a blood-pressure cuff to block arterial and venous blood flow. The cuff remained in-

flated for 60 s, after which the pressure was released, and the recording was continued for 5 min. The purpose of this experiment was to investigate the response of the PPG instrument to arrested blood flow and to detect possible differences between blood flows in the skin and bone tissue during post-occlusion reactive hyperemia.

2.3.4 Application of liniment

Liniment (Transvasin®, Seton Products, Oldham, UK) was applied to the surface of the skin over the patella to increase skin blood flow by vasodilator activity. The active substances in Transvasin (tetrahydrofurfursalicate, etylnikotinate, and hexylnikotinate) increase skin perfusion, and nicotinic acid has a dilating effect after a few minutes [29].

Photoplethysmographic recordings were performed for 60 s to establish a reference value. The probe was then removed, and a minor amount of liniment was quickly applied to the surface of the PD. After replacing the probe at the same site on the patella, PPG signals were acquired for another 5 min. The purpose of this experiment was to investigate the ability of the PPG instrument to differentiate between skin and bone blood flow when a substance known to induce skin vasodilatation was applied to the skin.

2.4 In vitro study of the PPG signal in a rigid tube

The rigid flow-through model consisted of a hole (diameter 2 mm) drilled in a piece of acrylic glass (PMMA). In the reflection mode of PPG an optical detecting fiber (diameter=1 mm) was placed adjacent to an illuminating fiber (diameter=1 mm) with a center-to-center distance of 2.5 mm and a distance of 2 mm between the fibers and the hole. A LED (wavelength 880 nm) was used as the light source for the illuminating fiber. The light from the detecting fiber was guided to a silicon PD (CERLED, Neumarkt, Germany). The measurements were performed on blood from 12 healthy blood donors, with hemoglobin (Hb) concentrations ranging from 116 to 162 g/l.

The blood was circulating in a silicon tubing system described earlier [19]. A waveform generator regulated a roller pump (Mekaneljo, Lund, Sweden), which produced a simulated pressure waveform closely resembling the human pulsatile blood pressure [5, 19]. Blood flow in ml/min was determined by collecting the blood for 60 s at each pressure level. Measurements were made with both whole blood and hemolyzed blood.

2.5 Statistical analysis

The statistical package Statistica 7.1 (StatSoft Inc., Tulsa, USA) was used for statistical analysis of the data obtained described under 2.3. Mean values and standard deviations (SDs) were calculated for the anthropometric data. For statistical analysis, the mean value of the individual bilateral measurements was used. Differences in blood flow between individual pairs, based on assessments before and after intervention, are expressed as percent of pre-intervention control, and the results are given as medians, SDs, and ranges. Wilcoxon's paired signed rank test was used to test for differences between blood flow in skin and bone tissue. The level of significance was set at $P < 0.05$. In the physical model (2.4) the correlation coefficient was determined using a computer program (MATLAB 7.0) to assess the association between the PPG signal and the blood pressure.

3 Results

3.1 Measurements of PPG signals on the patella

Figure 6 shows a typical PPG recording from bone (804 nm) and skin (560 nm) at rest in one subject. There was a slow variation in baseline of the skin PPG signal but not in the corresponding signal from bone tissue.

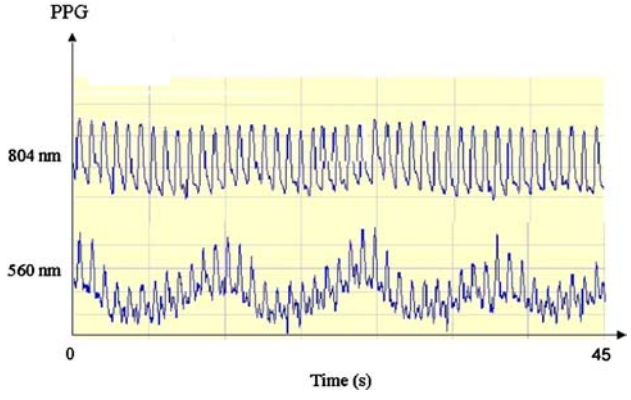

Fig. 6 Typical photoplethysmographic recordings from bone (804 nm) and skin (560 nm) at rest in one subject. Signals are in arbitrary units. The AC component is quantified as the pulse-by-pulse amplitude average over 20 consecutive pulsations. Note the difference in baseline between the two *curves*; the slow-wave shift at 560 nm is likely to reflect autoregulatory activity in the skin whereas such activity is not evident in the recording at 804 nm. The amplifications have been adjusted to the same magnitude

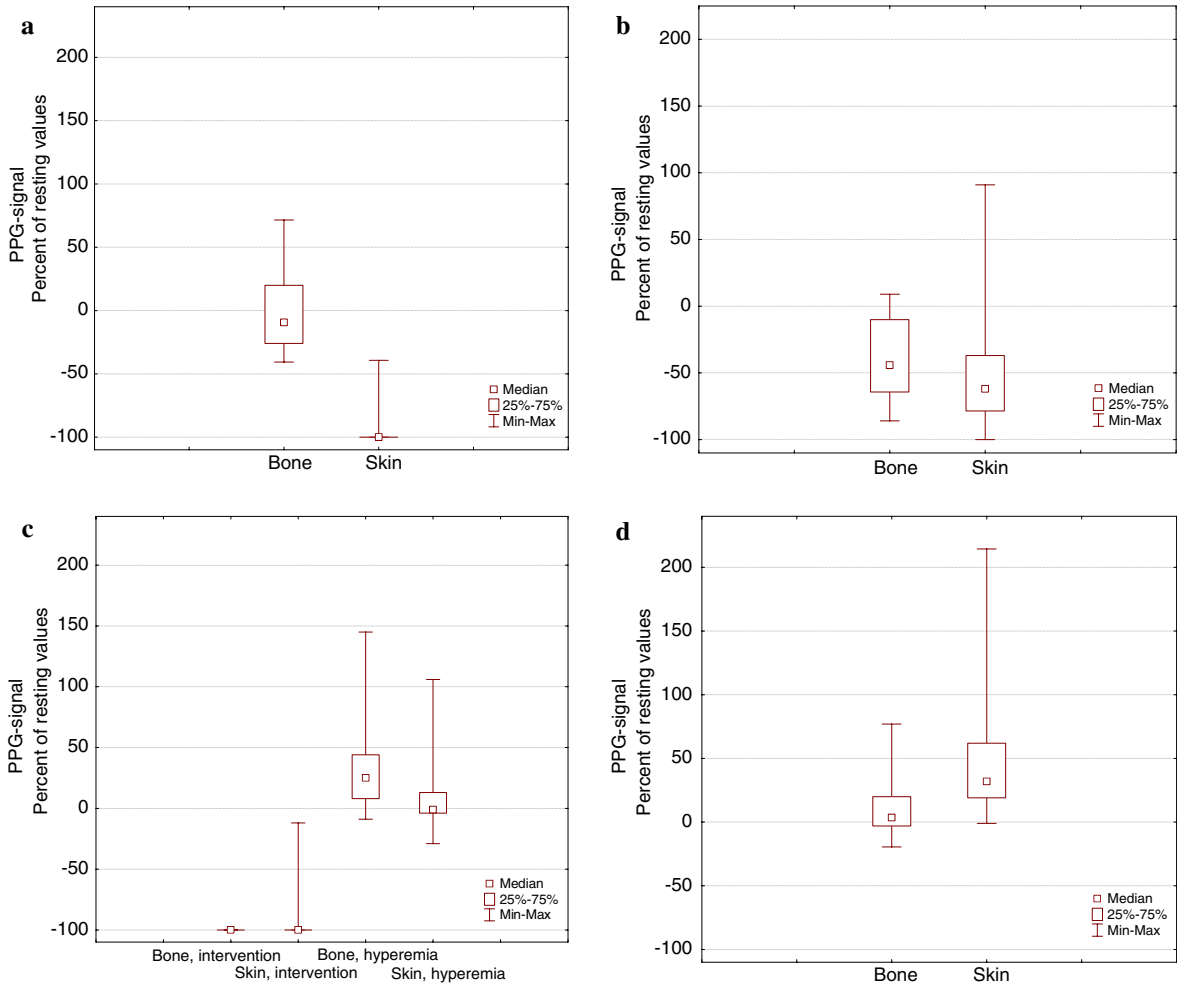

Fig. 7 a–d Changes in the pulse-synchronous AC component of the photoplethysmographic signal from bone (804 nm) and skin (560 nm) tissues, during different interventions. The results are given as medians, SDs, and ranges. **a** Vascular occlusion of skin tissue (n=20). **b** Venous occlusion (n=20). **c** Arterial occlusion (n=17). **d** Application of liniment (n=19)

The amplitudes of the AC component during the interventions are presented in Fig. 7a–d. Values are expressed as percent of pre-intervention control. In the results, the mean values from the left and right knees are presented. Some recordings of the PPG signal was not analyzed due to 50 Hz noise and then the recordings from only one knee will be presented. In some interventions, fewer than 20 subjects were analyzed, also because of a high noise level in the PPG signal.

3.1.1 Vascular occlusion of skin tissue

The PPG signal from the skin over the patella (560 nm) was blocked after application of a local pressure of 100 mmHg. The signal from the patellar bone (804 nm) showed some influences from the skin occlusion but was not significantly decreased (P=0.63). There was a significant difference in the signals from the tissues ($P<0.001$) (Fig. 7a).

3.1.2 Venous occlusion

During venous occlusion, a significant decrease in both signals was found (bone, $P<0.001$; skin, P=0.001). The signal from the skin decreased more than the signal from the bone (P=0.052) (Fig. 7b).

3.1.3 Arterial occlusion

The PPG signals from the skin and the patella were absent during arterial occlusion. After the pressure was released, a significant increase, compared with baseline, was seen in the signal from the patella ($P<0.001$) but not from the skin (P=0.54), and the difference

between the signals of the two tissues was significant (P=0.02) (Fig. 7c).

3.1.4 *Application of liniment*

After liniment was applied, the PPG signal from the skin increased significantly ($P<0.001$) while the increase in the signal from the bone was non-significant (P=0.07). There was a significant difference between the signals of the two tissues ($P<0.001$) (Fig. 7d).

3.2 In vitro study of the PPG signal in a rigid tube

Figure 8 shows relative changes in the PPG AC-signal when the pulsatile pressure was varied between 0 and 100 mmHg, superimposed on a constant diastolic pressure of 70 mmHg, and at a constant frequency of 1 Hz (corresponding to 60 beats/min). The blood flow (ml/min) through the rigid tube varied linearly with the intra-tube pressure (Fig. 9). The experiments were performed using both whole- and hemolyzed blood from the same donors. With whole blood the PPG AC-signal varied with the pressure pulse. Plotting the values from PPG AC-recordings against the pulsatile pressure, the correlation coefficient was 0.82. With hemolyzed blood no pulsatile signals were recorded.

4 Discussion

This paper presents and evaluates a non-invasive optical technique for assessing changes in pulsatile blood flow in human bone tissue utilizing PPG. The results indicate the potential of the method for monitoring local bone blood flow, although with some limitations that will be discussed below. In order to assess the performance of the probe we chose interventions with relatively well-established consequences for skin and bone tissue.

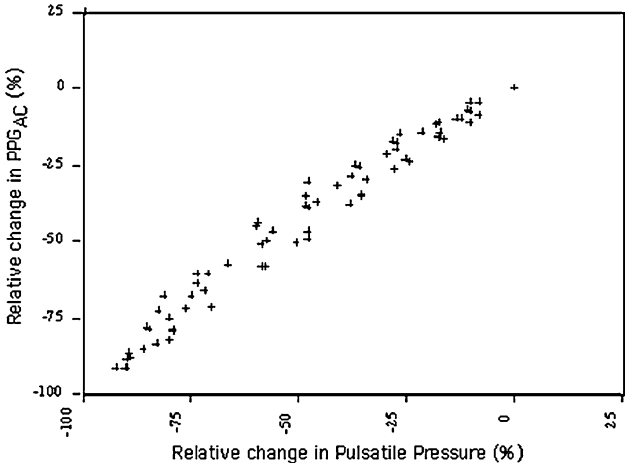

Fig. 8 The AC component of a photoplethysmographic signal (PPG_{AC}) as a function of the pulsatile blood pressure in a hydraulic model. In the model whole blood is circulated with a pump where diastolic and pulsatile pressures can be simulated. The PPG signal is obtained in reflection mode from a rigid, transparent tube, where the flow varies in proportion to the pressure (Fig. 9)

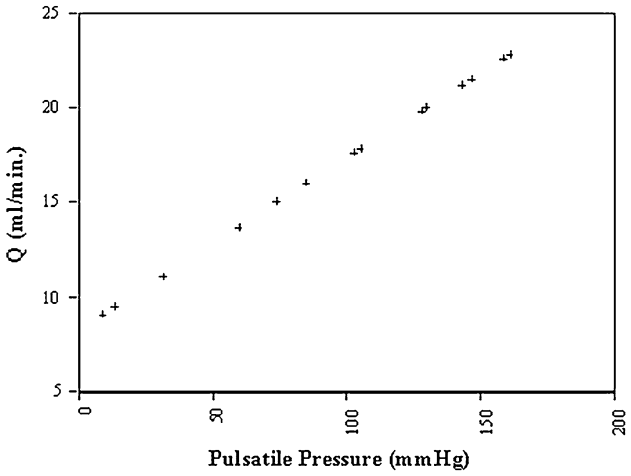

Fig. 9 Mean blood flow (Q) as a function of pulsatile blood pressure in model described in Fig. 8

4.1 Human measurements

In several experiments slow variations in blood flow were observed in skin perfusion but not in bone perfusion (Fig. 6). The frequency of these slow variations was in the range 4–8/min which corresponds to the frequency of autoregulation [17, 23]. These findings actually demonstrate the ability of this probe to discriminate between skin and bone compartments.

Vascular occlusion of skin tissue by application of local pressure confirmed that the PPG signal at 560 nm originated mainly from the skin tissue. There was also a reduction in the PPG signal at 804 nm. It was, however, significantly less than the reduction at 560 nm, suggesting that blood flow can be measured from a vascular compartment beneath the compressed skin tissue and that inflow of blood to the patellar bone occurs in part through arteries penetrating the patellar surface below the compressed probe.

Venous occlusion with a cuff pressure of 60 mmHg result in a complete arrest of venous flow, at least during the initial phase of the occlusion [13]. During a 1-min venous occlusion, perfusion in the occluded tissues between arterial inflow and the occluded veins is most likely incompletely arrested, since all vascular compartments are first completely filled with venous blood, after which the arterial pressure is transmitted

to the site of venous occlusion so that some degree of venous flow is re-established [32]. Our present finding of partial reductions in PPG signals from both the skin and the patellar bone—by 50% or more—are thus compatible with a partial reduction of tissue flow in both compartments.

Arterial occlusion should be complete at a cuff pressure of 180 mmHg in our normotensive, supine subjects with the knee at the level of the heart. We observed a complete cessation of pulse-synchronous PPG signals from bone tissue in all subjects, and from skin tissue in 15 of 17 subjects. The remaining two subjects had extremely large thigh circumferences for which the largest available cuff probably was not wide enough. Also, the PPG signal from bone tissue increased significantly after the pressure was released, which is compatible with a modest reactive hyperemia following the relatively short period of occlusion. The findings made during and after arterial occlusion indicate that the PPG signal reflects tissue blood flow.

Application of liniment was expected to influence blood flow mainly in the skin. Accordingly, we observed a higher PPG signal from the skin after the application of liniment, while the PPG signal from bone tissue was not influenced.

4.2 Physical model of rigid vessel

As seen in Fig. 8 there is a close linear relationship between changes in AC-signals and changes in pulsatile blood pressure. Despite great variations in Hb concentration (Hb 116–162), which certainly affects the blood viscosity and therefore the orientation capability of the RBC [10], the AC-signal was shown to reflect variations in the pulsatile pressure and flow in a rigid tube that permits no changes in the volume of the illuminated blood.

4.2.1 Blood volume shifts vs. blood flow pulsations as a source of the AC component of the PPG signal

The present results obtained with the physical vessel model, and studies on PPG and the dental pulp, support the notion that flow pulsations can give rise to variations in heart-synchronous PPG signals in rigid blood flow channels [22]. An alternative interpretation of the pulsatile component of the PPG signal from rigid tissue compartments such as the patellar bone and dental pulp would be that there are rhythmic alterations between the relative contents of arterialized and desaturated venous blood with an increase in the arterialized component during each systolic inflow into the rigid compartment. In the present study, this explanation is unlikely, since measurements from the bone tissue were obtained with light at a wavelength of 804 nm, where light absorption of arterial and venous blood is equal (the isobestic point).

The present technique to perform continuous and non-invasive blood flow measurements in bone tissue may be used to investigate the basic pathophysiology of many bone disorders. Further development of the new PPG technique should focus on validating the probe so that measurements will be reliable and absolute in all accessible areas of the human skeleton. Since the PPG method is non-invasive, its advantage over invasive methods is that it can be used in studies on humans. To date, several angiographic studies of intraosseous blood supply in the human knee joint have been published [2, 15, 31]. However, these methods cannot be used to continuously study blood flow during provocations or during repeated measurements over time. Iida et al. [15] found that ischemic bone marrow disorders such as osteonecrosis in the knee are likely to develop in areas with lower blood volume. In bone, ischemia sometimes stimulates remodeling and neovascularization. It has been shown that exposure to intermittent normobaric hypoxia results in distinct tissue remodeling [26]. Prolonged ischemia may cause cell death. Ischemia is reported to be responsible for osteonecrosis. Osteoporosis and osteoarthritis are also reported to be linked to atheromatous vascular disease [7].

The most obvious limitation of the present technique is the lack of gold standard to calibrate it against. Thus, results at this stage can only be shown as relative changes from one point in time to another.

5 Conclusions

The results of this study indicate that changes in the blood flow in human trabecular bone tissue can be assessed continuously and non-invasively using a new custom-designed PPG probe.

Acknowledgments The authors wish to thank Per Sveider and Bengt Ragnemalm for technical assistance, Iréne Lund for statistical advice, and Erik Lundeberg for preparing some of the illustrations.

References

1. Anetzberger H, Thein E, Becker M, Zwissler B, Messmer K (2004) Microsphere accurately predicts bone blood volume. Clin Orthop Relat Res 424:253–265

2. Arnoldi CC (1991) Patellar pain. Acta Orthop Scand 62(Suppl. 244):12–13
3. Binzoni T, Leung T, Hollis V, Bianchi S, Fasel JH, Bounameaux H, Hiltbrand E, Deply D (2003) Human tibia bone marrow: defining a model for the study of haemodynamics as a function of age by near infrared spectroscopy. J Physiol Anthropol Appl Human Sci 22:211–218
4. Bonutti PM, Miller BG, Cremen MJ (1998) Intraosseous patellar blood supply after medial parapatellar arthrotomy. Clin Orthop Relat Res 352:202–214
5. Borgström P, Clementz LA, Grande PO (1981) A servo-controlled roller pump for constant flow or constant pressure blood perfusion under normal pulsatile or non-pulsatile conditions. Acta Physiol Scand 112:437–442
6. Challoner AVJ (1979) Photoelectric plethysmography for estimating cutaneous blood flow. In: Rolfe P (ed) Non-invasive physiological measurements, vol. 1. Academic, London, pp. 125–151
7. Conaghan PG, Vanharanta H, Dieppe PA (2005) Is progressive osteoarthritis an atheromatous vascular disease? Ann Rheum Dis 64:1539–1541
8. Dye SF (1993) Imaging of the knee. Orthop Rev 22:901
9. Dye SF, Campagna-Pinto D, Dye CC, Shifflett S, Eiman T (2003) Soft-tissue anatomy anterior to the patella. J Bone Joint Surg Am 85:1012–1017
10. Fujii M, Nakajima K, Sakamoto K, Kanai H (1999) Orientation and deformation of erythrocytes in flowing blood. Ann N Y Acad Sci 873:245–261
11. Gelfer Y, Pinkas L, Horne T, Halperin N, Alk D, Robinson D (2003) Symptomatic transient patellar ischemia following total knee replacement as detected by scintigraphy. A prospective, randomized, double-blind study comparing the mid-vastus to the medial para-patellar approach. Knee 10:341–345
12. Graaf R, Dassel A, Koeölink M, de Mul F, Aarnoudse J, Zilstra W (1993) Optical properties of human dermis in vitro and in vivo. Appl Opt 32:435–437
13. Groothuis JT, van Vliet L, Kooijman M, Hopman MT (2003) Venous cuff pressures from 30 mmHg to diastolic pressure are recommended to measure arterial inflow by plethysmography. J Appl Physiol 95:342–347
14. Hughes SS, Cammarata A, Steinmann SP, Pellegrini VD (1998) Effect of standard total knee arthroplasty surgical dissection on human patellar blood flow in vivo: an investigation using laser Doppler flowmetry. J South Orthop Assoc 7:198–204
15. Iida S, Harada Y, Ikenoue S, Moriya H (1999) Measurement of bone marrow blood volume in the knee by position emission tomography. J Orthop Sci 4:216–222
16. Kamal A, Harness J, Irving G, Mearns A (1989) Skin photoplethysmography—a review. Comput Methods Programs Biomed 28:257–269
17. Larsen PD, Hary M, Thiruchelvam M, Galletly DC (1997) Spectral analysis of AC and DC components of the pulse photoplethysmograph at rest and during induction of anaesthesia. Int J Clin Monit Comput 14:89–95
18. Lindberg LG, Öberg PÅ (1991) Photoplethysmography. Part 2. Influence of light source wavelength. Med Biol Eng Comput 29:48–54
19. Lindberg LG, Öberg PÅ (1993) Optical properties of blood in motion. Opt Eng 32:253–257
20. Loaiza LA, Yamaguchi S, Ito M, Ohshima N (2002) Electroacupuncture stimulation to muscle afferents in anesthetized rats modulates the blood flow to the knee joint through autonomic reflexes and nitric oxide. Auton Neurosci 97:103–109
21. Lustig JP, London D, Dor BL, Yanko R (2003) Ultrasound identification and quantitative measurement of blood supply to the anterior part of the mandible. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 96:625–629
22. Miwa Z, Ikawa M, Iijima H, Saito M, Takagi Y (2002) Pulpal blood flow in vital and nonvital young permanent teeth measured by transmitted-light photoplethysmography: a pilot study. Pediatr Dent 24:594–598
23. Nitzan M, de Boer H, Turivnenko S, Babchenko A, Sapoznikov D (1994) Power spectrum analysis of spontaneous fluctuations in the photoplethysmographic signal. J Basic Clin Physiol Pharmacol 5:269–276
24. Nitzan M, Babchenko A, Khanokh B (1999) Very low frequency variability in arterial blood pressure and blood volume pulse. Med Biol Eng Comput 37:54–58
25. Notzli HP, Swiontkowski MF, Thaxter ST, Carpenter GK, Wyatt R (1989) Laser Doppler flowmetry for bone flow measurements: helium–neon laser light attenuation and depth of perfusion assessment. J Orthop Res 7:413–424
26. Rakusan K, Ehrenburg I, Gulyaeva N, Tkatchouk E (1999) The effect of intermittent normobaric hypoxia on vascularization of human myometrium. Microvasc Res 58:200–203
27. Reynolds KJ, Moyle JT, Gale LB, Sykes MK, Hahn CE (1992) In vitro performance test system for pulse oximeters. Med Biol Eng Comput 30:629–635
28. Sakamoto K, Kanai H (1979) Electrical characteristics of flowing blood. IEEE Trans Biomed Eng 26:686–695
29. Sandberg M, Lindberg LG, Gerdle B (2004) Peripheral effects of needle stimulation (acupuncture) on skin and muscle blood flow in fibromyalgia. Eur J Pain 8:163–171
30. Sandberg M, Zhang Q, Styf J, Gerdle B, Lindberg LG (2005) Non-invasive monitoring of muscle blood perfusion by photoplethysmography: evaluation of a new application. Acta Physiol Scand 183:335–343
31. Scapinelli R (1967) Blood supply to the human patellae. J Bone Joint Surg Br 49:563–570
32. Wilkinson IB, Webb DJ (2001) Venous occlusion plethysmography in cardiovascular research: methodology and clinical applications. Br J Clin Pharmacol 52:631–646
33. Zhang Q, Lindberg LG, Kadefors R, Styf J (2001) A non-invasive measure of changes in blood flow of the human anterior tibial muscle. Eur J Appl Physiol 85:567–571