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Original Article

Hylonome

In vivo measurements of human bone deformation using optical segment tracking: surgical approach and validation in a three-point bending test

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Abstract

The purpose of the study was to validate optical segment tracking, a new method for *in vivo* human tibia deformation measurements and to assess bending in a three-point bending test. The approach relies upon optical motion capturing of reflecting marker clusters affixed to the bone via screws inserted three millimeters into the corticalis in local anesthesia. The method was tested in five healthy subjects. Screws were left in place for six to eight hours and a variety of exercises performed. A pain questionnaire was used to assess pain levels. PQCT-images were taken to locate screw holes in the bone. A three-point bending test was performed and repeatability evaluated. The new method shows good feasibility though this was previously considered impossible by many experts. Local anesthesia works for screw implantation and explantation. Results show linearity with an average of 0.25 degrees per 10 kg of weight applied with good repeatability (average variation coefficient 8%). Optical segment tracking is feasible for human *in vivo* bone deformation measurements. There is a variety of possible clinical and experimental applications including stability testing of osteosyntheses and joints, monitoring of bone healing, evaluation of exercises in physiotherapy, and assessment of bone deformation patterns in bone disease.

Keywords: Motion Capturing, Visual Analog Scale, Bone Deformation, pQCT, Three-point-bending

Introduction

A body of literature is available on *in vivo* bone deformation measurements in animals and humans[1-3]. Measuring bone deformation is informative in many ways, be it for an estimate of musculoskeletal forces or for an assessment of the risk to fracture[4]. Classically such measurements are based on strain gauge recordings, an approach that has several drawbacks[5-7]. From a scientific point of view, strain gauges give information on a small part of the bone in one axis, as well as shear strain, rather than reflecting whole-bone deformation. Several strain gauges have to be combined on opposing surfaces to assess bending. From a technical perspective, strain gauges are difficult to bond to bone, and no method exists that would reflect the quality of bonding. Furthermore, this method is quite invasive as incisions of five to ten centimeters in lengths and removal of the periosteum as well as de-greasing and cleaning of the bone surface are necessary prior to strain-gauge application. Extensometers using K-wires and bone staples with strain gauges are currently state of the art in *in vivo* bone strain measurements[8,9]. The development of these methods resolved the bonding problem of the strain gauge approach. Limitations of these methodological approaches, however, include reduced accuracy and difficulty to achieve 3-dimensional information of global bone strain distribution and torsion. It would therefore be of interest to extend the spectrum of available measurement techniques. Some of the open questions that cannot be addressed with the available methods have recently been pointed out by Yang et al[5].

The authors have no conflict of interest.

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For these reasons, the authors have devised a new method that relies upon optical assessment of marker clusters affixed to the bone via screws, called optical motion tracking[10]. Bone deformation can be computed from the relative displacement between clusters. This method has proven to capture precise and minute movement of markers with a resolution of <20 µm in a volume of 400x300x300 mm^3, and the next step was to apply the method *in vivo* during physical activity, and to thus assess bone function in healthy volunteers. Effectiveness of the new method has been tested previously, but repeatability and feasibility need to be proven[10]. While discussing the new approach with a number of colleagues prior to setting up this particular study, it was heavily criticized for probably being very painful and therefore not suitable *in vivo*. Of note, the optical method described here is less invasive than strain gauge recordings[8,11]. Our experience with external fracture fixation and K-wire treatment was that pain is not a problem once pins are inserted, and that insertion should be possible in local anesthesia. One aim of the study was therefore to test and document feasibility from a pain point of view. Concerning screw stability, we had good results in cadaveric animal bone, but we were unsure if the same would apply to *in vivo* human bone. Screws have previously been inserted in the tibial condyle of healthy human volunteers to mount accelerometers, however in a different location and combined with less intensive exercise[12]. For bone staples, an insertion depth of two to four millimeters was proven to be suitable for *in vivo* bone strain measurements in previous studies[8,11]. Intra-cortical bone pins have also been used to measure tibiofemoral kinematics[13].

The purpose of the first *in vivo* measurements presented in this paper was to evaluate feasibility and repeatability of optical segment tracking for *in vivo* bone deformation measurements in humans, and to measure tibia deformation in a three point bending test.

Materials and methods

Study setting

Ethical approval was obtained both from the ethics committee of North Rhine Medical Association (No. 2011306) and from the ethics committee of Cologne University Hospital (No. 12-007). Informed consent was obtained from all subjects.

Subject selection included a questionnaire, blood tests (standard pre-operative laboratory tests including parameters for infection and coagulation), HIV and Hepatitis B and C-tests, urine analysis, ECG and clinical examination. Inclusion criteria were male gender, age between 20 and 55 years, body mass Index (BMI) between 20 and 30 kg/m^2 as well as agreement and signed consent forms before the study. Exclusion criteria included being an employee of the performing institutions, a reaction or serious event following any type of anesthesia in the past, thickness of ventral tibia cortex below 4 mm between 20 and 80% of the tibia's length, muscle or joint disease, bone fracture less than one year prior to the study, participation in another clinical study within the last two months, history of increased bleeding (hemophilia, regular use of anticoagulants) and any other condition that is considered potential risk by the study's executive medical director[5,11].

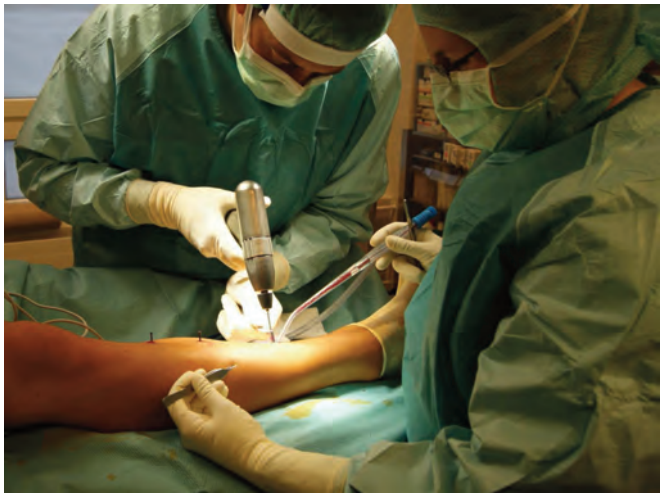


Figure 1. Drilling prior to insertion of the distal bone screw. Two screws are already in place. Both procedures, screw insertion and screw extraction, were performed under sterile conditions in an orthopedic operation theatre.

For all experiments subjects were trained and familiarized in so-called *dry-runs* with sham-markers. In addition, MRI scans were performed prior to the experiment day to assess cortical thickness of the tibia and to plan marker positioning accordingly.

To minimize risk of infection, experiments were carried out in two operation theatres, one used for screw implantation and explantation, and another for the experiments. The tests described in this manuscript were part of a larger protocol that included walking, running on a treadmill, jumping, squatting, a three-point bending test and others. Screws were implanted at 8 am and explanted before or at 6 pm.

Screw implantation

30 minutes previous to screw implantation, Ibuprofen 600 mg and Cefuroxime 1500 mg were administered. A choice was given between local anesthesia and a combination of local anesthesia with a short general anesthesia for both the insertion and explantation of screws. However, an anesthetist was present even when the test subject declined general anesthesia. Local anesthesia was performed with a mixture of long- and short-lasting local anesthetic to receive immediate onset as well as a long lasting effect. Xylocain 1% and Carbostesin 0.5% were injected in the skin until the subject reported numbness. Next, the periosteum was infiltrated with the same combination of local anesthetic. The procedures of screw implantation and explantation were performed under sterile surgical conditions (Figure 1). Three screws were inserted into the ventral aspect of the right tibia at: (i) approximately 10 cm

distal of the tibia plateau, (ii) in mid-shaft and (iii) approximately 10 cm proximal from the medial malleolus. To control the depths of screw insertion intraoperatively, the number of rotations of the screw's thread were counted given the distance between threads was known. A skin incision of 1 cm in length is necessary for each screw. Sterile plasters were applied around the screw to minimize risk of infection (Figure 2). After screw removal, intracutaneous resorbable stitches were applied to the wounds.

Stryker Asnis Micro 3.0 mm cannulated titan screws (self cutting screw, Ø3 mm, 24 mm total length, 6 mm thread length, Stryker Leibinger GmbH & Co. KG, Duisburg, Germany) were used for marker cluster fixation. New screws were used for each subject. Holes were drilled with a Stryker Asnis Micro solid drill (Ø2.1 mm, Stryker Leibinger GmbH & Co. KG, Duisburg, Germany). New drills were used for each subject to minimize friction and heat development. Previous testing in cadaveric cattle bone had shown that a depth of three millimeters is sufficient for stable screw insertion. Three custom-made marker clusters with three non-collinear retro-reflective markers each (diameter Ø5 mm, Géodésie Maintenance Services, Nort Sue Erdre, France) were then affixed to the bone screws (Figure 2).

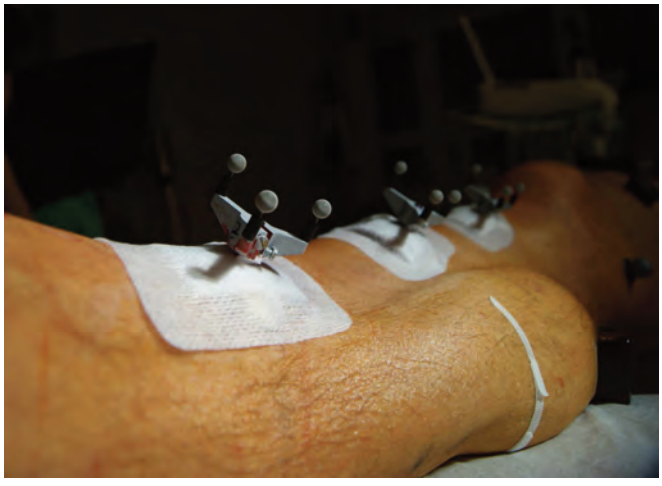


Figure 2. Marker clusters mounted on bone screws. The wound is covered by sterile plasters. A steri strip on the calf serves as marker for ultrasound measurements.

Data acquisition

During the exercises, trajectories of the markers were captured with the Vicon MX motion capture system (eight Vicon F40 cameras, Vicon Motion System Ltd., LA, USA) at 300 Hz, using infrared light. Tibia deformation angles, i.e. bending and torsion, were calculated based on the relative movement between markers. Screw stability was assessed just after screw implantation and before removal by measuring the resonance frequency obtained through flipping the marker with a finger[14].

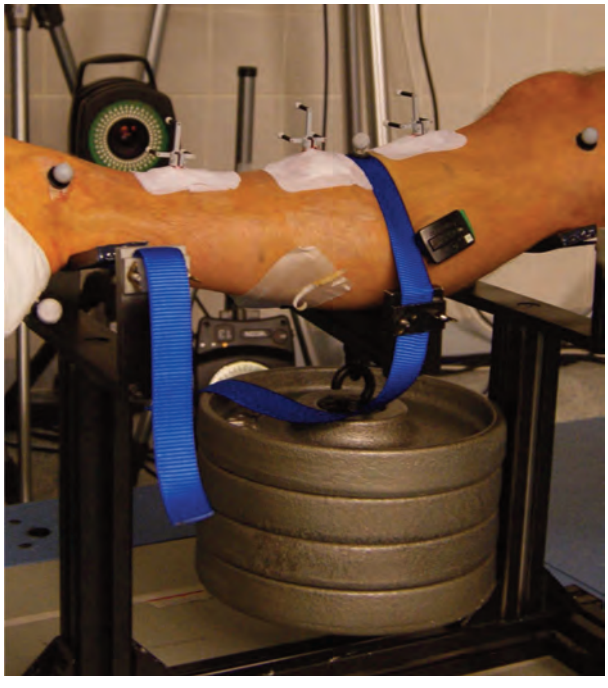


Figure 3. Setup of the three-point bending-experiment with 20kg of weight applied between the proximal and medial screw.

Pain

The pain treatment scheme was based on the World Health Organization's analgesic ladder[15]. In addition to local anesthesia and, if chosen, short general anesthesia, the following medications were available for oral application: Subjects took a tablet of Ibuprofen 600 mg 15 minutes before screw insertion. In case of pressure or pain sensation during the experiments, Metamizol (Novalgin®) 500 mg was given. More Ibuprofen was available if necessary. In case repetitive Metamizol in addition to Ibuprofen was not sufficient, oral Tramadol (Tramal®) 50 mg was applied.

Pain levels and description of the sensation were assessed by a questionnaire using a numerical scale (ranging from 0 for no pain to 10 for maximal pain) for each experiment, as well as open questions. The questionnaires were to be filled in in between experiments.

PQCT scans

To determine the exact position of the screws, peripheral Quantitative Computed Tomography (pQCT) scans were obtained as described before after the experiment day[16]. In one subject, another scan was done three months later to demonstrate bone healing and compare values for bone mineral density (vBMD), bone cross sectional area (CSA) and bone mineral content (BMC).

Three-point posterior bending test

In order to assess the repeatability of the proposed approach in bone deformation recording, a three-point bending test with

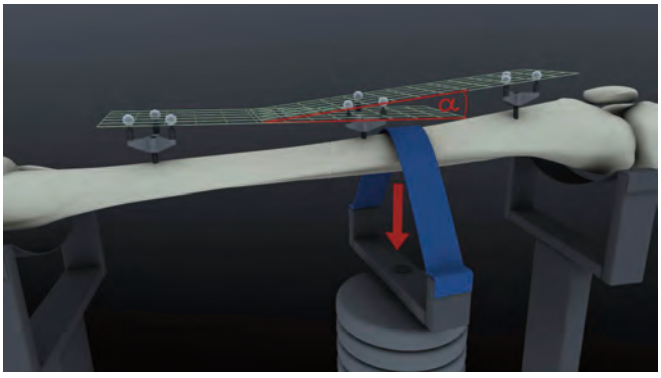
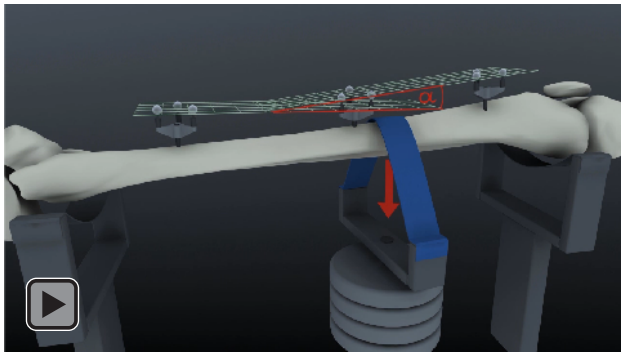


Figure 4. Draft of the deformation angle measured in the axis of weight application (rendered with Autodesk 3ds Max). Plains of the proximal and distal marker cluster are used to compute the deformation angle in the axis of force application.



Animation 1. The animation shows how bone deformation changes the angle measured in the three-point bending test.

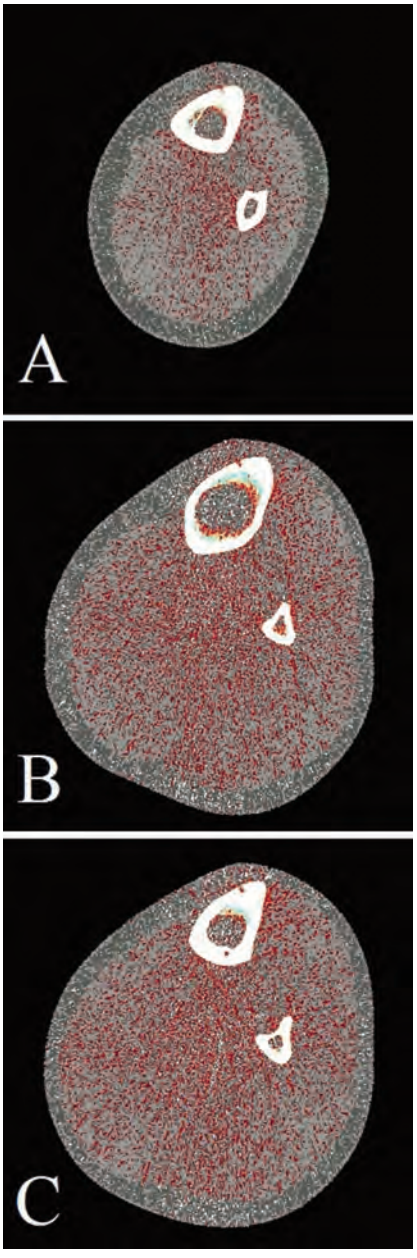


Figure 5A-C. PQCT-images of the lower leg in one subject four days after screw explantation (A=distal, B=midshaft, C=proximal). All images show the drilling channel clearly visible in the ventral aspect of the tibia. Drilling holes are in safe distance to the bone marrow.

10 and 20 kg of weight applied to the tibia positioned on distal and proximal support benches was performed (Figure 3). The bending angle caused by the applied weight was computed from the relative movement of marker clusters (Figure 4 and Animation 1). Matlab (The MathWorks, Inc. Version 7.9.0 R2009b) routines were written to process the marker's trajectories and calculate the deformation angle from the relative displacement between marker clusters. At least two repetitions were done in each subject with 10 and 20 kg of weight, respectively. A regression analysis was performed for each subject and for all measurements. P-values were calculated using t-test on the slope coefficient.

Results

Five male Caucasian subjects were recruited between 26 and 50 years of age (37.2 years +/-7.76), all matching the inclusion criteria mentioned above. Subjects were easily able to perform the exercises. Importantly, none of the screws loosened or broke. None of the five subjects had a fracture in the right tibia during the first year after the study. Measuring the resonance frequency of the screws showed identical patterns before and after the experiments, which means that screws did not loosen. The frequency remained at approximately 262 Hz.

Overall, no noticeable pain occurred in any of the exercises performed (Table 1). All subjects chose to have the screws inserted in local anesthesia without additional short general anesthesia. An anesthetist was available at all times, and subjects

Subject	**A**	**B**	**C**	**D**	**E**
Did you have pain on the experiment day or afterwards (yes/no)?	no	no	no	no	no
What did the screws feel like in your skin?	I have not felt anything	Unreal, I have only felt them when I looked at them	Funny pressure	No perception of screws	Not felt them, no pain
Pain on Visual analog scale with 0=no pain and 10=worst pain					
First operation (screw insertion)	0	0	0	**1**	0
Second operation (removal of screws)	**2**	0	0	0	0
Attaching and changing marker clusters	0	0	0	0	0
Standing	0	0	0	0	0
Sitting	0	0	0	0	0
Walking	0	0	0	0	0
Running	0	0	0	0	0
Walking stairs	0	0	0	**not performed#**	0
Heelraises and plantarflection	0	0	0	0	0
Standing with +40 kg of weight	0	0	0	0	0
Squats with +20 kg of weight	0	0	0	0	0
Three-point bending test	0	0	**1**	0	0
Walking with crutches	0	0	0	0	0
Jumping both legs	0	0	0	0	0
Jumping right leg	0	0	0	0	0
Drop-jump from 40 cm height	0	0	0	**not performed***	0
Vibration platform	**not performed***	0	0	**not performed***	0

Table 1. Answers in the pain questionnaire. *Not performed due to lack of time, # not performed due to technical problems.

had the option to have the short general anesthesia at any stage of the study. However, general anesthesia was not requested by any of the subjects, and all screws were inserted and explanted under local anesthesia. All subjects received Ibuprofen 600mg before screw insertion. Only two subjects received further pain relief during the day when describing a feeling of pressure in the shin. In both cases, Metamizol (Novalgin®) 500 mg was sufficient as a single dose to eliminate the perception of pressure. One subject mentioned a sting during the application of local anesthesia for screw insertion (pain level 1 out of 10). One subject furthermore experienced pain during screw removal caused by skin desinfection (pain level 2 out of 10). None of the experiments had to be interrupted due to pain or discomfort.

Bleeding only occurred in the first subject during the more vigorous activities such as jumping and hopping. Despite cauterization prior to screw insertion, several interruptions became necessary in order to change plasters. Cauterization was applied more thoroughly in the subsequent subjects. In addition, thin adhesive strips (Steri Strips®) were used to prevent skin movement and shearing of tissue at the screws. These procedures successfully reduced bleeding in the remaining four subjects to very low levels, and plasters had to be changed only once or twice during jumping.

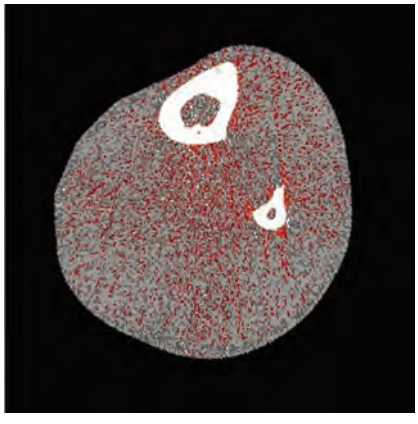


Figure 6. PQCT-image three months after the experiment (different subject than Figure 5). The screw hole is filled up again; mineral content in the hole is still decreased compared to the surrounding corticalis.

Wound healing was immediate, and no other problem such as

Location of slice	Area	Time of measurement	vBMD [mg/cm³]	CSA [mm²]	BMC [mg/mm]
Distal hole	**Total bone**	**Three days after experiment**	**973.5 +/- 5.0**	**440.2**	**428.5**
		Three months later	**974.7 +/- 5.0**	**442.1**	**430.9**
	Cortical bone	Three days after experiment	1168.1 +/- 9.0	361.1	421.8
		Three months later	1177.8 +/- 9.0	358.6	422.4
Proximal hole	**Total bone**	**Three days after experiment**	**601.9 +/- 5.0**	**921.1**	**554.4**
		Three months later	**605.3 +/- 5.0**	**910.2**	**550.9**
	Cortical bone	Three days after experiment	1018.9 +/- 9.0	483.5	492.6
		Three months later	1026.5 +/- 9.0	475.8	488.4

Table 2. Bone mineral density (vBMD), bone cross sectional area (CSA) and bone mineral content (BMC) in one subject three days after the experiment and three months later.

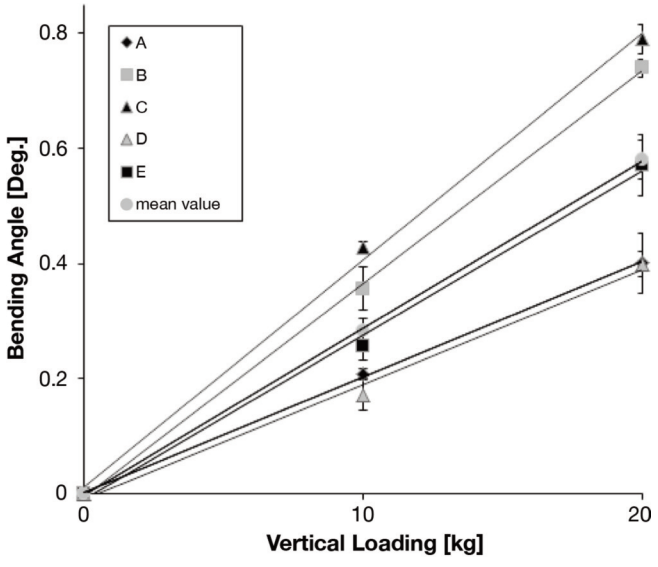


Figure 7. Plot of results for each subject including mean values, standard deviations and regression lines. The experiment was repeated at least twice for each weight and subject. Standard deviations are displayed for each measurement in each subject.

Data set	y	R^2	p-value
A	0.0194x+0.0142	0.891	0.079
B	0.0383x-0.0269	0.9834	0.002
C	0.0363x+0.0651	0.9944	<0.001
D	0.0227x-0.0539	0.9694	<0.001
E	0.0316x-0.0607	0.9445	<0.001
All data points	0.0249x+0.047	0.4882	<0.001

Table 3. Results from regression analysis. Y is the regression equation, R^2 the Coefficient of Determination and the p-value results from t-test on the slope coefficient.

infection or paresthesia was observed in any of the five subjects.

Cortical thickness was assessed by MRI-scans prior to the experiments and exceeded 4 mm in all subjects at the sites of screw implantation. PQCT-images confirmed position and depths of screw canals in the tibia after screw removal (Figures 5a-c). The bone marrow was not opened in any of the five cases, and the depth of the canal did not exceed 3mm. Three months later bone remineralization in screw canals is detectable (Figure 6). Values for bone mineral density (vBMD), bone cross sectional area (CSA) and bone mineral content (BMC) in one subject three days after the experiment day and three months later (Table 2). No systematic change can be found in these values.

Results from the three-point bending test suggest a linear correlation between the applied weight and the bending angles (Figure 7). The slope in values of the linear regression differs interindividually and varies by the factor two (Table 3). Figure 8 shows the vBMD (average of values at the three holes) plotted against the bending angle slope from the regression analysis. A linearity with an average bending of 0.25 degrees per 10 kg of weight applied results from the test. Repeatability of measurements has proven to be high as can be seen in the low standard deviation between the repetitions in each subject (Figure 7). The average variation coefficient is 0.076 (8%).

Discussion

The aim of this study was to evaluate feasibility and repeatability of optical segment tracking to *in vivo* bone deformation measurements in humans and to measure bending in a three-point bending test.

Due to ethical considerations, this pilot study was performed on five male subjects only, and a number of experiments were performed to achieve the maximum benefit. Optical segment tracking is an invasive method that involves risk of infection, screw loosening, screw breakage as well as

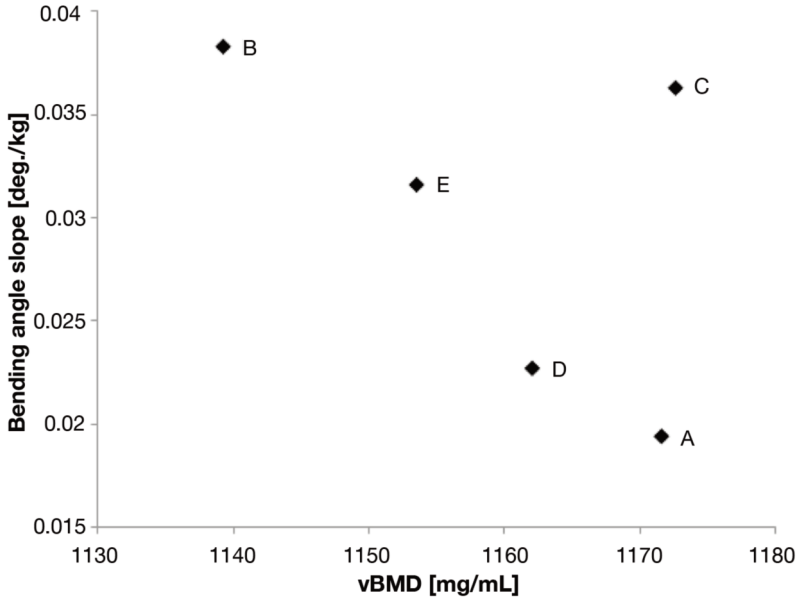


Figure 8. Plot of vBMD against the bending angle slope from the regression analysis.

injury to nerves and blood vessels. The number of subjects was sufficient to evaluate feasibility and repeatability of the new method. Of note, optical segment tracking is less invasive than conventional strain gauge measurements[5,7-9].

In the three-point bending test, the point of force application and the exact leg position on the support benches were not controlled. Furthermore, the leg's external and internal rotation was not identical while the bending angle was calculated in the direction of force application. These aspects are certainly weaknesses in this explorative study and should be addressed in the future though this is technically hard to achieve.

3 mm cannulated titan screws give sufficient stability for the optical markers, even when inserted only 3 mm into the cortical bone of the ventral tibia as previously expected[5]. The screws' resonance frequency remained stable during the experiment day which indicates that screws remain fixed in the bone. Procedures of screw insertion and explantation can well be performed in local anesthesia. It is crucial to carefully inject the local anesthetic initially into the skin followed by the periosteum. Only a small amount of oral pain medication is necessary for a variety of exercises including squats, running and jumps. Bleeding can be controlled by sufficient cauterization and the application of thin adhesive strips (Steri Strips®) in addition to sterile plasters applied to the wounds surrounding screws. If this is not done thoroughly, bleeding can be a problem during vigorous exercises such as hopping and jumping. Wound healing was immediate in all subjects of the present study and no infection occurred. Osteomyelitis is a major concern when opening the bone marrow[17]. In this study, we avoided opening of the bone marrow through screw insertion with a sufficient safety margin. This was achieved by prior MRI scans, planning and careful drilling into the ventral aspect of the tibia. From this perspective, one could say that the risk of infection has been minimized. However, our sample size (n=5) is too small to make any inference about the actual risk of infection, and it is therefore left to future studies to explore that risk. Likewise, whether or not screw insertion and explantation actually have to be performed in an operation theatre, or whether sufficient sterile surgical conditions could also be achieved by a less stringent set-up could be a relevant question in the future if our proposed approach finds its way into medical practice. We conclude from these observations that the proposed approach is well feasible. However, further risks need to be mentioned. In case of a fall, screws might theoretically break. In this case, it might be difficult to remove the part of the screw remaining in the bone. Sterile surgical instruments should be ready, and the subject should be informed on the procedure in this event. To decrease this risk, experiments should be practiced with the subjects in advance. Another risk is damage to anatomical structures such as nerves and blood vessels, especially in locations with more soft tissue cover than the ventral tibia. The risk of bone fracture, however, is probably not increased after application of this method as bones have a 'safety factor' for fracture risk in the order of magnitude of 10[18]. From a clinical experience point of view, the risk of subsequent fracture due to the holes in the load path of the tibial cortex should not be increased. The screws used were purposely smaller in diameter than the screws used in external fixation as a treatment for tibia fractures. In addition, screws were only inserted 3 mm into the cortex and did not penetrate it completely. After removal of screws in plate osteosynthesis, holes with a bigger diameter remain that penetrate the cortex fully. In our clinical routine, patients are allowed to put full weight on the leg. As removal of pins and plates is frequently done in our hospital, we would see fracture complica-

tions, and also fatigue fractures, if there were any. In our experience, tibia fractures after removal of pins and plates are extremely rare. The risk of fracture is higher when bone defects are larger, e.g. in tumor surgery or after bone biopsy. Keeping in mind that the screws in the present study had a much smaller diameter and did not fully penetrate the cortex, we consider the risk for subsequent fracture extremely low in healthy young subjects. We do, however, think that we cannot judge the risk in patients with osteoporosis or other bone disease such as osteogenesis imperfecta. In these cases, as well as in older patients, the application of the method might be limited, and risks need to be evaluated further before application in these patient groups is ethically rectifiable. Future subjects should be informed that there is a risk of fracture, and that they should get in contact with the study team if pain occurs in the area of screw implantation.

Results suggest good repeatability of measurements (variation coefficient 8%) which suggests even better values in more intensive exercises such as running and hopping. Repeatability needs to be re-assessed when applying the method to a different bone.

To the best of our knowledge, there have been no *in vivo* three-point bending tests of the human tibia before, and there has likewise not been any assessment of *in vivo* deformation angles in humans yet. Results of the three-point bending test show linearity with an average bending of 0.25 degrees per 10 kg of weight applied. High interindividual variance was found with the slope ranging from 0.19 degrees per 10 kg to 0.38 degrees per 10 kg. Interindividual differences in the deformation pattern could be caused by variations in the bone's material and structural properties, maybe changing with age and bone density. They can however as well be influenced by the varying relative position of the point of force application in relation to the bone screws in the experimental setup.

Optical segment tracking shows good practicability regarding the surgical technique, screw stability, pain, bleeding and wound healing. Screw implantation and explantation can be done in local anesthesia, and subjects can perform a large number of exercises with only a minimum of pain medication. Repeatability, efficacy and effectiveness have shown excellent results. The new method is therefore, also from a surgical point of view, superior to the more traditional strain gauge approach to *in vivo* bone deformation measurement. Relevant biomechanical data has been obtained that has the potential to yield important information also in clinical populations. The present study introduces a new techniques that broadens the spectrum of measurement options for *in vivo* bone deformation measurements. It might especially be of interest in combination with other data, e.g. from CT. The procedure permits the calculation of global strain between markers, and could enable for calculations of the strain field and of local bone strain by using finite element models. This could be achieved by integrating data on the bone shape and geometry (CT and MRI measurments) and deformation data. Possible applications include *in vivo* human bone deformation measurements and stability testing of osteosynthesis and joints, monitoring of bone healing in malunion, evaluation of exercises in physiotherapy and assessment of bone deformation patterns in bone disease (e.g. osteoporosis or osteogenesis imperfecta). In other words, this new method has potential to enhance current clinical practice.

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