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[Continued on next page]

(54) Title: SYSTEMS AND METHODS FOR ESTABLISHING THE STIFFNESS OF A BONE USING MECHANICAL RESPONSE TISSUE ANALYSIS

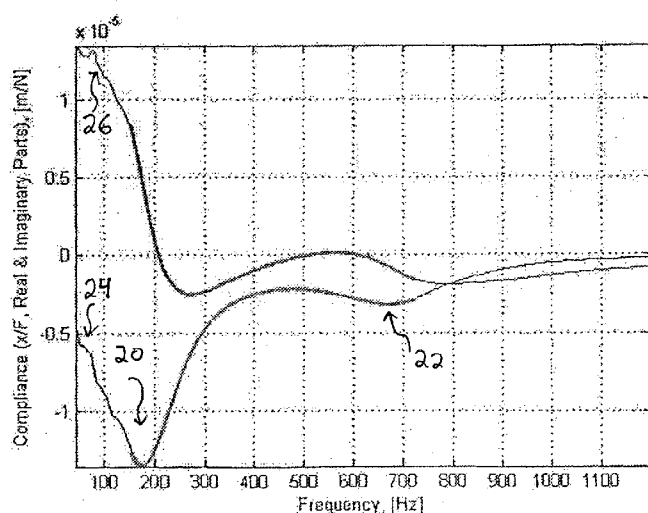


Fig. 3

(57) Abstract: Parametric model based computer implemented methods for determining the stiffness of a bone, systems for estimating the stiffness of a bone in vivo, and methods for determining the stiffness of a bone. The computer implemented methods include determining a complex compliance frequency response function $Y(f)$ and an associated complex stiffness frequency response function $H(f)$ and fitting a parametric mathematical model to $Y(f)$ and to $H(f)$. The systems include a device for measuring the stiffness of the bone in vivo and a data analyzer to determine a complex compliance frequency response function $Y(f)$ and an associated complex stiffness frequency response function $H(f)$. The methods for determining the stiffness include fitting a parametric model to stiffness of the skin-bone complex as a function of frequency $H(f)$ and the compliance of the skin-bone complex as a function of frequency $Y(f)$.

**Declarations under Rule 4.17:**

- *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*
- *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*
- *of inventorship (Rule 4.17(iv))*

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- *with international search report (Art. 21(3))*

(88) Date of publication of the international search report:
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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US14/33816

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61B 8/00, 8/14; G01S 15/89; G09B 23/30 (2014.01)

CPC - A61B 5/0048, 8/0875; G01S 19/23

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC(8): A61B 6/03, 8/00, 8/14, 17/58; G01S 15/89; G09B 23/30 (2014.01)

CPC: A61B 5/0048, 5/0051, 8/0875; G01S 7/52074, 15/8979, 15/8993, 19/23

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

MicroPatent (US-G, US-A, EP-A, EP-B, WO, JP-bib, DE-C,B, DE-A, DE-T, DE-U, GB-A, FR-A); Google/Google Scholar; ProQuest; Pubmed/Medline: bone, osseo, tissue, stiffness, hardness, vibratory, oscillatory, static, function, time, reduce, transform, mechanical, response, parametric, ulna, invert, complex, frequency, root mean square, hertz, hz

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y --- A	US 5006984 A (STEELE, CR) April 9, 1991; figures 1, 3-4; column 2, lines 23-29; column 3, lines 15-23; column 5, lines 51-57; column 6, lines 9-12, 20-29, 33-69; column 10, lines 41-56	1, 3, 5, 10-11, 13, 16, 30, 32, 37, 39-40 ----- 12 ----- 2, 4, 6-9, 14-15, 31, 33-36, 38
Y --- A	US 7485100 B2 (GARCIA-WEBB M et al.) February 3, 2009; column 6, lines 3-7; column 8, lines 8-21; column 15, lines 62-66	12 ----- 2, 4, 6-9, 14-15, 31, 33-36, 38
A	WO 2012/089221 A1 (VAIN, A) July 5, 2012; page 4, lines 29-35	2
A	COTTON, JR et al. "Ulna Simulation Assesses Sensitivity to Bone Elastic Modulus Variations in a MRTA test". Abstract presented at 2012 American Society of Biomechanics 36th Annual Meeting from Wednesday, 15 August 2012 to Saturday, 18 August 2012. Abstract saved online at http://www.asbweb.org/conferences/2012/topics/index.html between 5 October 2012 and 5 November 2012; pages 231-232.	2

☐ Further documents are listed in the continuation of Box C.

* Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier application or patent but published on or after the international filing date	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&" document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means	
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

28 August 2014 (28.08.2014)

Date of mailing of the international search report

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US14/33816

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I: Claims 1-16 and 30-40 are directed toward a method and a computer implemented method for determining stiffness of a bone.

Group II: Claims 17-29 are directed toward a system for determining stiffness of a bone in vivo.

-Continued Within the Next Supplemental Box-

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-16, 30-40

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

-Continued from Box No. III - Observations where unity of invention is lacking-

The inventions listed as Groups I-II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the special technical features of Group I includes (iv) fit a parametric mathematical model to $Y(f)$ to obtain a first set of parameters of the parametric mathematical model, including the stiffness of the bone (K_B), (v) fit the parametric mathematical model to $H(f)$ to obtain a second set of parameters of the parametric mathematical model, including the stiffness of the bone (K_B), which are not present in Group II; the special technical features of Group I includes to fit the parametric mathematical model to $Y(f)$ to obtain a first set of parameters of the parametric mathematical model, including the stiffness of the bone (K_s), to fit the parametric mathematical model to $H(f)$ to obtain a second set of parameters of the parametric mathematical model, including the stiffness of the bone (K_s), which are not present in Group I.

The common technical features of Groups I and II are a method for determining the stiffness of a bone, comprising: (1) applying a controlled superposition of static and oscillatory forces (F) measured as a first function of frequency $F(f)$ over a range of frequencies to a skin-bone complex in vivo, thereby exciting oscillatory accelerations (a) over the range of frequencies of the skin-bone complex; receiving the oscillatory forces as functions of time $F(t)$ and the oscillatory accelerations as functions of time $a(t)$; transforming $a(t)$ and $F(t)$ to functions of frequency, $a(f)$ and $F(f)$, to reduce $a(f)$ and $F(f)$ to acceleration frequency response data $A(f)$; to determine a complex compliance frequency response function $Y(f)$ and associated complex stiffness frequency response function $H(f)$; to determine the discrepancies between the first set of parameters and the second set of parameters as a measure of conformity thereof to the parametric mathematical model.

These common technical features are disclosed by US 5,006,984 A (STEELE). Steele discloses a method (the method is based on the calculation of physical parameters, i.e. is parametric; column 1, lines 59-67) for determining the stiffness of a bone (the method is used to determine stiffness of bone; column 2, lines 40-44), comprising: (1) applying a controlled superposition of static (a static force is maintained the tissue; figure 2; column 6, lines 53-64) and oscillatory forces (F) measured as a first function of frequency $F(f)$ (a vibratory (oscillatory) force is also applied to the tissue; figure 2; column 6, lines 40-52) over a range of frequencies to a skin-bone complex in vivo (the forces are applied to tissue region 46 over a range of frequencies; figure 2; column 6, lines 2-9, 40-52), thereby exciting oscillatory accelerations (a) over the range of frequencies of the skin-bone complex (the forces are applied over a range of frequencies to develop an acceleration over the range of frequencies; figures 1-2; column 1, lines 51-59; column 5, lines 66-69); receiving the oscillatory forces as functions of time $F(t)$ and the oscillatory accelerations as functions of time $a(t)$ (the forces applied to the mass and the deflection (acceleration) are received as derivatives (functions) of time; column 9, lines 20-32); transforming $a(t)$ and $F(t)$ to functions of frequency, $a(f)$ and $F(f)$ (the two inputs are transformed using a fast Fourier transform to determine components over (as a function of) high and low ; frequencies; column 5, lines 59-65), to reduce $a(f)$ and $F(f)$ to acceleration frequency response data $A(f)$ (the two inputs are plotted as frequency-dependent response data reduced as a function of excitation frequency; column 6, lines 2-10); to determine a complex compliance frequency response function $Y(f)$ (a complex compliance value curve, i.e. function, is determined; column 10, lines 41-46) and associated complex stiffness frequency response function $H(f)$ (associated bone stiffness parameters are calculated from this compliance value using related equations; column 10, lines 41-46); to determine the discrepancies between the first set of parameters and the second set of parameters as a measure of conformity thereof to the parametric mathematical model (the refined parametric values are compared with the previously estimated values (prior model) to determine convergence (conformity with the model); column 10, lines 64-67).

Since the common technical features are previously disclosed by the Steele reference, the common features are not special and so Groups I and II lack unity.