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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte PUNEET SHARMA, LUCIAN MIHAI ITU, BOGDAN GEORGESCU, VIOREL MIHALEF, ALI KAMEN, and DORIN COMANICIU

Appeal 2018-002114
Application 13/672,781
Technology Center 2100

Before ERIC B. CHEN, MATTHEW R. CLEMENTS, and SCOTT E. BAIN, *Administrative Patent Judges*.

CHEN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134(a) from the final rejection of claims 1–43, which constitute all the claims pending in the application. We have jurisdiction under 35 U.S.C. § 6(b). We reverse.

INVENTION

Appellants' invention, a "method and system for multi-scale anatomical and functional modeling of coronary circulation" (Title), provides a "patient-specific anatomical model of coronary arteries and the heart . . . generated from medical image data of a patient" (Abstract). "The predictive nature of the multi-scale coupled model of the coronary circulation is intrinsically linked to its coupling with cellular models[, which] makes it possible to track the initiation, and subsequent growth of coronary plaques and their effect on the overall circulation." (Spec. ¶ 46.)

Claim 1 is exemplary, with disputed limitations in italics:

1. A method, comprising:

generating a patient-specific anatomical model of coronary arteries and a heart from medical image data of a patient;

generating a multi-scale functional model of coronary circulation based on the patient-specific anatomical model;

coupling, to the multi-scale functional model of coronary circulation, *a cellular model of endothelial cell function that simulates changes in a mechanical property of a vascular wall due to a response of endothelial cells to hemodynamic forces,* wherein a wall shear-stress value calculated by the multi-scale functional model of coronary circulation is used to couple the multi-scale functional model of coronary circulation to the cellular model of endothelial function through a mechanotransduction model; and

simulating blood flow in at least one stenosis region of at least one coronary artery and changes in a mechanical property of a vascular wall in the at least one stenosis region of the at least one coronary artery due to a response of endothelial cells in the vascular wall to hemodynamic forces from the simulated blood flow using the multi-scale functional model of coronary circulation and the cellular model of endothelial cell function

coupled to the multi-scale functional model of coronary circulation.

EXAMINER'S REJECTIONS

Claims 1–5, 7–12, 15–19, 21–25, 27–34, and 36–43 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Taylor (US 2012/0041739 A1; Feb. 16, 2012), Ionasec (US 2010/0070249 A1; Mar. 18, 2010), and NIH[1] (C.A. Taylor et al., *Open Problems in Computational Vascular Biomechanics: Hemodynamics and Arterial Wall Mechanics*, 198 COMPUT. METHODS APPLIED MECH. & ENG'G. 3514–3523 (2009)). (Final Act. 11–38.)

Claims 6, 26, and 35 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Taylor, Ionasec, NIH, and Passerini (T. Passerini et al., *A 3D/1D Geometrical Multiscale Model of Cerebral Vasculature*, 64 J. ENG'G MATH 319–330 (2009)). (Final Act. 38–40.)

Claim 13 stands rejected under 35 U.S.C. § 103(a) as unpatentable over Taylor, Ionasec, NIH, and Naghavi (US 2011/0270051 A1; Nov. 3, 2011). (Final Act. 40–43.)

Claim 14 stands rejected under 35 U.S.C. § 103(a) as unpatentable over Taylor, Ionasec, NIH, and Algranati (D. Algranati et al., *Mechanisms of Myocardium-Coronary Vessel Interaction*, 298 AM. J. PHYSIOLOGY-HEART & CIRCULATORY PHYSIOLOGY, H861–H873 (2010). (Final Act. 44–45.)

Claim 20 stands rejected under 35 U.S.C. § 103(a) as unpatentable over Taylor, Ionasec, NIH, and Holzapfel (G. Holzapfel et al., *A Layer-Specific Three-Dimensional Model for the Simulation of Balloon*

[1] Accessed as an author manuscript from the National Institutes of Health.

Angioplasty Using Magnetic Resonance Imaging and Mechanical Testing, 30 ANNALS OF BIOMEDICAL ENG'G. 753–767 (2002)). (Final Act. 45–48.)

ANALYSIS

§ 103 Rejection—Taylor, Ionasec, and NIH

We are persuaded by Appellants' arguments (App. Br. 7–8; *see also* Reply Br. 5–7) that the combination of Taylor, Ionasec, and NIH would not have rendered obvious independent claim 1, which includes the limitation "a cellular model of endothelial cell function that simulates changes in a mechanical property of a vascular wall due to a response of endothelial cells to hemodynamic forces."

The Examiner found that the description of hypertension in NIH, the description of arterial hemodynamic conditions in NIH, and the development of multiscale models (e.g., endothelial dysfunction) in NIH, collectively correspond to the limitation "a cellular model of endothelial cell function that simulates changes in a mechanical property of a vascular wall due to a response of endothelial cells to hemodynamic forces." (Final Act. 19; *see also* Ans. 8–10.) We do not agree with the Examiner's findings.

NIH relates to "highlighting[] some past successes of vascular biomechanics, but emphasizes the need for research that synthesizes complementary advances in molecular biology, biomechanics, medical imaging, computational methods, and computing power for purposes of increasing our understanding of vascular physiology and pathophysiology." (Abstract.) With respect to pulmonary hypertension, NIH explains that "[t]his form of the disease occurs primarily due to an increased vasoconstriction followed by significant remodeling of the walls of medium-

and small-diameter arteries." (§ 3.2, para. 3.) With respect to arterial hemodynamic conditions, NIH explains that "[a]rteries retain a remarkable ability to adapt to changing hemodynamic conditions throughout life" and "[t]he best known examples are that arteries increase (or decrease) in caliber in response to sustained increases (or decreases) in blood flow induced wall shear stresses and they increase (or decrease) in thickness in response to sustained increases (or decreases) in blood pressure." (§ 4.5, para. 1 (footnotes omitted).) Moreover, in the "Open Problems" section, NIH explains that "there is a need to begin to develop multiscale models that combine knowledge of molecular mechanisms with clinical manifestation," and "subclasses of such models [fluid-solid-growth models] are possible and should be pursued for specific clinical problems based on dominate underlying processes (e.g., endothelial dysfunction)." (§ 5.4.)

The Examiner cited to: (i) the description in NIH of pulmonary hypertension, including vasoconstriction; (ii) the description in NIH of arterial hemodynamic conditions; and (iii) multiscale models of NIH, which combine molecular mechanisms with clinical manifestation, for example, endothelial dysfunction. The Examiner, however, has provided insufficient evidence to support a finding that NIH teaches the limitation "a cellular model of endothelial cell function that simulates changes in a mechanical property of a vascular wall due to a response of endothelial cells to hemodynamic forces." In particular, the Examiner has not demonstrated that the concepts of vasoconstriction, arterial hemodynamic conditions, and endothelial dysfunction correspond to "a cellular model of endothelial cell function that simulates changes in a mechanical property of a vascular wall due to a response of endothelial cells to hemodynamic forces," as recited in

claim 1. Moreover, NIH explains that "there is a need to begin to develop multiscale models" relating to endothelial dysfunction, which is an indication that such models were not yet developed at the time of NIH. (§ 5.4; *see also* Abstract.) We are, therefore, persuaded by Appellants' arguments that:

> [S]ection 5 of NIH_2009 describes open problems that have not yet been solved, and section 5.4 describes that "advances in molecular biology and systems biology promise to enable modeling of underlying mechanobiology (i.e., mechanotransduction, . . ." Accordingly, this section states that such a model of underlying mechanobiology is an expected advance in the future, but does not describe a cellular model of endothelial function that can be coupled to a multi-scale model of coronary circulation. . . . As described in section 3.2 of NIH_2009, pulmonary hypertension occurs primarily due to an increased vasoconstriction followed by significant remodeling of the walls of medium and small diameter arteries. However, there is no description of any cellular model that simulates such changes in a vascular wall due to a response of endothelial cells to hemodynamic changes. Section 4.5 of NIH_2009 describes vasoactive molecules that regulate vasodilation and vasoconstriction, but again, there is no description of a cellular model that simulates changes in a mechanical property of a vascular wall due to a response of endothelial cells to hemodynamic changes.

(App. Br. 8.)

Accordingly, we do not sustain the rejection of independent claim 1 under 35 U.S.C. § 103(a). Claims 2–5, 7–12, 15–19, 21, 22, and 41–43 depend from claim 1. We do not sustain the rejection of claims 2–5, 7–12, 15–19, 21, 22, and 41–43 under 35 U.S.C. § 103(a) for the same reasons discussed with respect to claim 1.

Independent claims 23 and 32 recite limitations similar to those discussed with respect to claim 1. We do not sustain the rejection of claims

23 and 32, as well as its dependent claims 24, 25, 27–31, and 33–40, for the same reasons discussed with respect to claim 1.

§ 103 Rejection—Taylor, Ionasec, NIH, and Passerini

Claims 6, 26, and 35 depend from independent claims 1, 23, and 32, respectively. The Examiner cited Passerini for teaching the additional features of claims 6, 26, and 35. (Final Act. 38–40.) However, the Examiner's findings regarding Passerini do not cure the above noted deficiencies of Taylor, Ionasec, and NIH.

§ 103 Rejection—Taylor, Ionasec, NIH, and Naghavi

Claim 13 depends from independent claim 1. The Examiner cited Naghavi for teaching the additional features of claim 13. (Final Act. 41–43.) However, the Examiner's findings regarding Naghavi do not cure the above noted deficiencies of Taylor, Ionasec, and NIH.

§ 103 Rejection— Taylor, Ionasec, NIH, and Algranati

Claim 14 depends from independent claim 1. The Examiner cited Algranati for teaching the additional features of claim 14. (Final Act. 44–45.) However, the Examiner's findings regarding Algranati do not cure the above noted deficiencies of Taylor, Ionasec, and NIH.

§ 103 Rejection— Taylor, Ionasec, NIH, and Holzapfel

Claim 20 depends from independent claim 1. Holzapfel was cited by the Examiner for teaching the additional features of claim 20. (Final

Act. 45–48.) However, the Examiner's findings regarding Holzapfel does not cure the above noted deficiencies of Taylor, Ionasec, and NIH.

DECISION

The Examiner's decision rejecting claims 1–43 is reversed.

REVERSED