Drawing Lines: The Boundary of Patentability in Personalized-Medicine Diagnostics (*)

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A correlation-based medical diagnostic is a diagnostic technology that is enabled by the discovery of a previously unknown correlation between an observable attribute of a patient (e.g., a genetic mutation) and a medically useful fact about, or diagnosis of, a patient (e.g., an inability to metabolize a drug). Correlation-based medical diagnostics are both commercially important and socially valuable because they are essential to the development of personalized or precision medicine.

Patent protection for many correlation-based medical diagnostics is available today in Japan. However, the reasons why many correlation-based medical diagnostics are patentable have not been clearly articulated, and thus the precise line between patentable and unpatentable correlation-based medical diagnostics remains uncertain. This report offers a number of theories about what the limits on the patentability of correlation-based medical diagnostics might be and thus where the line between patentable and unpatentable correlation-based medical diagnostics might be drawn. More specifically, it focuses on the restrictions that the diagnostic-method exclusion of the industrial-applicability requirement and both the laws of nature and mental activities exclusions of the statutory-invention requirement place on the patentability of correlation-based medical diagnostics.

I Introduction

A correlation-based medical diagnostic is a diagnostic technology that is enabled by the discovery of a previously unknown correlation between an observable attribute of a patient and a medically useful fact about the patient. Upon the discovery of previously unknown correlations between an observable attribute of a patient and a medical fact about that patient, researchers in the United States were historically able to obtain patent protection for a two-step diagnostic method with patent claims that recited (a) the step of determining if a patient possesses the attribute and (b) the step of mentally inferring that the medical fact is true if the patient possesses the attribute. Correlation-based medical diagnostics are socially and commercially valuable because they are essential components of the development of personalized medicine, which is also sometimes called precision medicine.

Patent protection for correlation-based medical diagnostics is, today, widely available in Japan, but there is no convincing explanation of how the line between patentable and unpatentable diagnostics is being drawn. Motivated by recent cases issued by the Supreme Court and Federal Circuit court of Appeals in the United States that radically decreased the amount of patent protection that is available for correlation-based medical diagnostics, this report articulates theories about the current state of patent law in Japan that explain why correlation-based medical diagnostics are patentable and where the line between patentable and unpatentable diagnostics lies. It focuses on two provisions in Japanese patent law that might, at first glance, be expected to invalidate patents on correlation-based medical diagnostics: the exclusion of method of diagnosis of humans under its industrial-applicability requirement and both the laws of nature and mental activities exclusions of the statutory-invention requirement.

II The Technology: Correlation-Based Medical Diagnostics and Personalized Medicine

1 What Is a Correlation-Based Medical Diagnostic?

A correlation-based medical diagnostic is a medical technology that is enabled by the discovery of a new correlation between an observable attribute of a patient (“the attribute”) and a medically relevant fact about a patient (“the medical fact”). Once such a correlation has been discovered, a new diagnostic technology has been created. The new diagnostic test has only two basic steps. First, a medical professional determines whether a patient has the attribute. Second, if patient possess the attribute, then the medical professional mentally reasons, or infers, the medical fact about the patient.

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2 Examples of Patents on Correlation-Based Medical Diagnostics

[omitted]

III Industrial Applicability in Japan

This section examines the patentability of correlation-based medical diagnostics under the industrial applicability requirement of Article 29 in Japan, which the Japanese Patent Office (JPO) has interpreted in its Examination Guidelines (Guidelines) to make medical activity, including methods of diagnosis of humans, industrially inapplicable inventions.

1 The Policy Concerns

[omitted]

2 The JPO Examination Guidelines

(1) Medical Activities Are Not Industrially Applicable

The Guidelines articulate a broad exclusion of "medical activity" from industrially applicable inventions, with "medical activity" being defined as "methods of surgery, therapy, or diagnosis of humans."[1]

(2) Defining the Category of Industrially Inapplicable Methods of Diagnosis of Humans

With respect to methods of diagnosis, the Guidelines offer the following definition of the excluded subject matter: "'Methods of diagnosis of humans' include methods of judging for [] medical purpose[s] the physical condition of a human body such as diseases and physical health, the mental condition of a human body, or prescription or treatment/surgery plans based on th[is] condition[]." [2] A 2009 revision to the Guidelines broadened the reach of patentability in the field of medical diagnostics. Most importantly, this revision states that "methods of analyzing" the data extracted from the human body by, for example, "comparing such … data with standards" are not inherently methods of diagnosis and thus can be industrially applicable.[3]

3 Application of the Guidelines to Correlation-Based Medical Diagnostics

This Section addresses the patentability of correlation-based medical diagnostics under the provisions in the Guidelines outlining the exclusion of medical activity from industrial applicability.

(1) Correlation-Based Medical Diagnostics Can Be Either Industrially Applicable or Inapplicable

(i) Methods of Diagnosis: No Industrial Applicability

The definition of methods of diagnosis in humans clearly envisions that some correlation-based medical diagnostics are inventions that are not capable of industrial application. For example, consider again the one and only case offered to illustrate an industrially inapplicable method of diagnosis: "Methods of judging whether the patient has had a stroke by observing the image obtained by the MRI scan."[4] Assuming that such a method would, in its detailed form, indicate that certain features or markings on an MRI scan mean that a patient has had a stroke, this claim can easily be re-written as a correlation-based medical diagnostic. That is, it could be rewritten as "a method of judging whether a patient has had a stroke comprising (a) determining whether certain features or markings are present on an MRI scan and (b) inferring that a patient has had a stroke if the features or markings are present." If the exclusion of methods of diagnosing humans is to have any impact at all, this simple reformulation of Case 1 must remain industrially inapplicable.

(ii) Data-Gathering Methods: Industrial Applicability

The Guidelines also clearly provide an example of a correlation-based medical diagnostic that is an industrially applicable method of analyzing samples or data about the human body: a method of determining susceptibility to hypertension discussed above as a case illustrating methods of analyzing extracted samples and data by, for example, comparing them with standards.[5] It is a classic example of a correlation-based medical diagnostic. The first step involves determining whether a patient has a particular attribute, namely whether the patient's X gene has an A or a G on the n^{th} line of the base sequence. The second step then involves inferring that the patient's susceptibility to hypertension is low if there is an A and high if there is a G.

(2) The Reason the Line is Difficult to Draw

The inclusion of methods of analyzing extracted samples and data by, for example, comparing them with standards within industrially applicable inventions makes the line at the boundary of medical activity difficult to draw when patents claim correlation-based medical diagnostics. After the inclusion of this category, assigning a medical meaning to data extracted from the body is the essence of both industrially inapplicable methods of diagnosis of humans, but it can also be the essence of industrially inapplicable methods of gathering data about the human body.

(3) Drawing the Line at the Boundary of Industrial Applicability

Based on the examples provided in the Guidelines, some, but not all, correlation-based medical diagnostics are industrially applicable in Japan today. This section

therefore articulates, at and times evaluates, a number of theories as to how Japanese patent law could draw the needed line.

(i) Semantics: Analyzing or Determining Versus Diagnosing or Judging

One possibility is that the line between industrially applicable and inapplicable correlation-based diagnostics boils down to semantics, i.e., to the words that a patent drafter uses when writing the claim. Under this theory, a claim that employs the terms "judging" or "diagnosing" is industrially inapplicable, whereas a claim that uses works like "examining," "analyzing," or "determining" is industrially applicable. Alternatively, the semantic line could be a one-way rule: using the wrong words will lead to a rejection for a lack of industrial applicability but simply using the right words will not automatically lead to industrial applicability.

(ii) Deterministic Reasoning Versus Experiential Judgment

Another way to draw the needed line would be to distinguish industrially applicable diagnostics that employ logical, analytically precise reasoning and that are capable of being expressed as a precise algorithm, on the one hand, from industrially inapplicable diagnostics that employ experiential judgment and that are impossible to codify in a precise algorithm, on the other hand. Here, the industrial applicability requirement would roughly sort the unpatentable "art" of diagnosis of humans from the patentable "science" of methods of analyzing extracted samples and data.

(iii) Final Diagnoses Versus Objective Data Supporting Final Diagnoses

Another way to interpret the Guidelines would be to draw a distinction between industrially inapplicable tests that generate information that definitively diagnoses the health of a patient, on the one hand, and industrially applicable tests that merely provide objective, factual information that only is used as an input into any definitive diagnosis the health of a patient that a doctor may eventually make, on the other hand. In other words, tests that reach a conclusion about a patient's health may be industrially inapplicable while tests that merely reveal information about the physiological state of the patient's body may be industrially applicable.

(iv) Laboratory Technicians Versus Medical Doctors

Another way to draw the needed line looks not at the objective nature of the judgment being made but rather at the identity person who is most likely to be tasked with performing the correlation-based medical diagnostic. What is the profession of the likely infringer? If the method is the type of method that is likely to be performed today by a technician in a clinical laboratory given the current market structure, then perhaps it is an industrially applicable method of analyzing samples or data. However, if the method is today likely to be performed by a medical doctor, then perhaps it is an industrially inapplicable method of diagnosing humans.

(v) International Harmonization as the Goal

A final theory about where the line between industrially applicable and industrially inapplicable correlation-based medical diagnostics lies assumes that the JPO's 2009 Guideline revisions were intended to bring Japanese patent law on medical diagnostics into line with patent law in the European Patent Office on medical diagnostics. Perhaps the expansion in patentability of diagnostics methods in the 2009 revisions to the exclusion of medical activities was meant to mirror the expansion that had occurred a number of years earlier in the European Patent Office.

IV Patentable Subject Matter in the US

Recent developments in United States have radically decreased the patent protection that is available for correlation-based medical diagnostics. More specifically, courts in the United States have interpreted Section 101 of the Patent Act to exclude correlation-based medical diagnostics from patentable subject matter for two independent reasons: they are both laws of nature and mental processes in the abstract.

1 Section 101 and Patentable Subject Matter

In a series of cases in the 1970s and 1980s, the United States Supreme Court interpreted Section 101 to codify several exclusions from statutory subject matter, holding that natural phenomena (i.e., products of nature), laws of nature, abstract ideas, and mental processes are not patentable subject matter within the four categories listed in the statute.[6] After several decades of inactivity, the Supreme Court recently returned to the issue of patentable subject matter in a series of cases stretching from 2010 to 2014.[7] These more recent cases clarified the methodology for drawing the difficult line between non-statutory claims to unpatentable subject matter itself and patentable processes that applied the unpatentable subject matter. More specifically, the Court held that one key step in this methodology was determining the part of the claimed invention that embodies the "inventive concept" or advance over the prior art.[8]

2 Judicial Interpretations of Section 101 Invalidating Correlation-Based Medical Diagnostics

Within the last several years, both the Supreme Court and the Federal Circuit have invalidated claims to

correlation-based medical diagnostics for failure to recite patentable subject matter under Section 101.

(1) The Laws of Nature Exclusion

The Supreme Court's decision in *Mayo Collaborative Services v. Prometheus Laboratories* is the leading case that explains why a patent on a correlation-based medical diagnostic is an unpatentable law of nature under section 101.[9]

(2) The Mental Processes Exclusion

The Federal Circuit opinion in *In re BRCA1- and BRCA2-Based Hereditary Cancer Test Patent Litigation* demonstrates how the Supreme Court's recent opinions on patentable subject matter suggest that patents on correlation-based medical diagnostics are unpatentable mental processes under section 101.[10]

V Statutory Inventions in Japan

Japanese patent law has a statutory-invention requirement codified in Article 2(1) stating that an invention is a "creation of technical ideas utilizing a law of nature."[11] Section 101 in the United States and Article 2(1) in Japan are similar on paper, but they produce radically different outcomes in practice when they are brought to bear on patents on correlation-based medical diagnostics. Although such patents are regularly invalidated for lack of patentable subject matter in the United States, they are unquestioningly assumed to be statutory inventions in Japan today. In the absence of judicial opinions, Guidelines, or scholarly commentary explaining why patents on correlation-based diagnostics describe neither unpatentable laws of nature as such nor unpatentable mental activities, this section offers some theories about how Japanese patent law might draw the line between statutory and non-statutory inventions in this technological area.

1 Article 2(1) and Statutory Inventions

The Guidelines attempt to create some clarity in this requirement by reciting a list of non-statutory inventions.[12] Most importantly for the present argument, the list includes two types of subject matters that do not utilize a law of nature. First, a law of nature as such is not a statutory invention.[13] Second, mental activities are not statutory inventions.[14]

2 Why Are Correlation-Based Medical Diagnostics Statutory Inventions?

This section offers provisional theories to explain why correlation-based medical diagnostics are unquestioningly presumed to be statutory inventions under Article 2(1) in Japan.

(1) The Laws of Nature Exclusion

In theory, there are two possible reasons why patents on correlation-based medical diagnostics might not be patents on laws of nature as such in Japan: either the newly discovered correlations that enable the methods are not laws of nature, or, if they are, the patents do not claim the correlations "as such." It is likely the latter reason that explains the difference between United States and Japanese treatment of correlation-based medical diagnostics. The Japanese definition of a claim to a law of nature "as such" is likely very narrow.

(2) The Mental Activities Exclusion

Again, in theory, there are two distinct reasons why a patent on a correlation-based medical diagnostic might not be labeled as a patent on a mental activity in Japan: either steps like comparing and inferring are not mental activities as that term is used in the Guidelines, or, if they are, the claimed invention nonetheless utilizes laws of nature when it is considered as a whole because the initial determining step is a technical, statutory step. Here, either one of these reasons may be sufficient to explain the difference between the application of the doctrine of patentable subject matter in the United States and the statutory-invention requirement in Japan.

(i) What Is a Mental Activity?

This report addresses two different theories about why mental processes are not statutory invention and thus two different definitions of inventions that implicate mental processes under Japanese patent law.

A first, plain-meaning theory more or less tracks the definition of a mental process in the United States and thus encompasses any activity that can be performed in a human mind. Under this theory, the inferring step in a correlation-based medical diagnostic is clearly a mental activity.

However, a second theory posits a much narrower definition of a mental activity and suggests that the inferring step of a correlation-based medical diagnostic is not a mental activity and is thus a statutory invention even in isolation. In gross, this theory proposes that the normative justification of the mental-activity exclusion of Article 2(1) is that *non-repeatable* processes should not be patentable. The Guidelines state that mental activities are excluded from patentability because they are examples of subject matter that fail to utilize a law of nature.[15] One of the classic hallmarks of an invention that utilizes a law of nature is that the invention must be repeatable in the sense that it is always able to attain the same effect. So, perhaps the Guidelines are only narrowly referring to non-repeatable mental activities when they identify the category "mental activities" that is excluded from statutory inventions. Under the non-repeatability theory, thought processes that occur within the human

mind are not mental activities as that phrase is used as a term of art in patent law if they are repeatable, algorithmic processes that model the laws of the natural sciences. The non-repeatability theory transforms repeatability from a necessary condition for a statutory invention—a non-repeatable creation is not a statutory invention—into a sufficient condition—any creation that is repeatable is a statutory invention, even if the creation exists only as a logical process within a human mind.

The Intellectual Property High Court embraced a variant of this non-repeatability theory of mental activities in the course of allowing a patent as a statutory invention in its well-known Bilingual Dictionary Case.[16]

(ii) When Does an Invention that Includes a Mental Activity Utilize a Law of Nature?

Assuming that the inferring step of a claim to a correlation-based medical diagnostic does recite a mental activity, the claim may still recite a statutory invention in Japan if it is a "mixed" claim—a claim that recites both a step that is a mental activity and other steps that recite technical, extra-mental activities. Because the existence of a statutory invention is judged by looking at the claim as a whole, the presence of the technical steps in the claimed method mean that the claim as a whole does not recite a mental activity. However, the Guidelines do not give a clear explanation of the conditions under which a claimed invention as a whole does or does not utilize a law of nature. Three different theories for making the needed distinction are raised as possibilities: the "any technical element" theory, the "inventive concept" theory, and the "centrality" theory. The recent Interactive Dental Network opinion authored by the Intellectual Property High Court suggests that Japan has adopted the centrality theory,[17] but further clarification is still needed for a definitive answer.

VI Conclusion

Motivated by recent cases issued by the Supreme Court and Federal Circuit Court of Appeals in the United States that radically decreased the amount of patent protection that is available for correlation-based medical diagnostics, this report examines the patentability of such diagnostics in Japan under both the industrial-applicability requirement and the statutory-invention requirement. Patent protection for correlation-based medical diagnostics is today widely available in Japan, but the reasons why this patent protection is available have not been clearly articulated. The line between patentable and unpatentable correlation-based medical diagnostics therefore remains uncertain. This report offers a number of possible theories to explain why this patent protection is available and suggests a number of lines that may function as the boundary of patent protection.

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1 JPO Examination Guidelines, Chapter 2.1.1 [hereinafter JPO Guidelines], https://www.jpo.go.jp/tetuzuki_e/t_tokkyo_e/1312-002_e.htm.
2 *Id.* at 2.1.1.1(3).
3 *Id.* at 2.1.1.2(3)(a).
4 *Id.* at 2.1.1.1(3).
5 *Id.* at 2.1.1.2(3)(a), Case 5.
6 Diamond v. Diehr, 450 U.S. 175 (1981); Diamond v. Chakrabarty, 447 U.S. 303 (1980); Parker v. Flook, 437 U.S. 584 (1978); Gottschalk v. Benson, 409 U.S. 64 (1972).
7 Bilski v. Kappos, 561 U.S. 593 (2010); Mayo Collaborative Servs. v. Prometheus Labs., 132 S.Ct. 1289 (2012); Ass'n for Molecular Pathology v. Myriad Genetics, 133 S.Ct. 2107 (2013); Alice Corp. Pty. Ltd. v. CLS Bank Int'l, 134 S.Ct. 2347 (2014).
8 *Mayo*, 132 S.Ct. at 1297–98; *Alice*, 134 S.Ct. at 2357–59.
9 Mayo Collaborative Servs. v. Prometheus Labs., 132 S.Ct. 1289 (2012).
10 *In re* BRCA1- and BRCA2-Based Hereditary Cancer Test Patent Litig., 774 F.3d 755 (Fed. Cir. 2014).
11 Tokkyohô [Japanese Patent Law], Law No. 121 of 1959, Article 2(1).
12 JPO Guidelines, *supra* note 1, at 1.1.
13 *Id.* at 1.1(1).
14 *Id.* at 1.1(4).
15 *Id.* at 1.1(4).
16 Intellectual Property High Court, Decision of August 26, 2008, Hanrei Jiho, No. 2031 – *Bilingual Dictionary Case*.
17 Intellectual Property High Court, Decision of June 24, 2008, 2007 (Gyo-Ke) 10369 – *Interactive Dental Network Case*.