

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 28

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES

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Ex parte CATO T. LAURENCIN, SAADIQ EL-AMIN,  
ARCHEL M. A. AMBROSIO, SHAWN R. PUCHER  
and HARRY R. ALLCOCK

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Appeal No. 1997-2634  
Application 08/222,662<sup>1</sup>

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HEARD: November 16, 2000

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Before ROBINSON, SPIEGEL and SCHEINER, Administrative Patent Judges.

SCHEINER, Administrative Patent Judge.

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<sup>1</sup> Application for patent filed April 4, 1994.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 1 through 4 and 10 through 13, all the claims remaining in the application. Claims 1 and 10 are reproduced as an Appendix to this opinion.

The references relied on by the examiner are:

Schacht et al. (Schacht)	5,104,947	Apr. 14, 1992
Lee	5,306,305	Apr. 26, 1994 <sup>2</sup>
Elia et al. (Elia)	5,380,329	Jan. 10, 1995 <sup>3</sup>

Laurencin et al. (Laurencin), "Use of Polyphosphazenes for Skeletal Tissue Regeneration," Journal of Biomedical Materials Research, Vol. 27, pp. 963-973 (1993).

The claims stand rejected as follows:

- I. Claims 1, 3, 10 and 12 under 35 U.S.C. § 103 as unpatentable over Elia, Laurencin and Schacht.
- II. Claims 2 and 11 under 35 U.S.C. § 103 as unpatentable over Elia and Laurencin.
- III. Claims 4 and 13 under 35 U.S.C. § 103 as unpatentable over Elia, Laurencin, Schacht and Lee.

We reverse all three rejections.

DISCUSSION

The specification describes a "synthetic material[] for bone repair and replacement, . . . particularly a poly(organophosphazene) three dimensional matrix." Specification, page

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<sup>2</sup> Application for patent filed January 31, 1992.

<sup>3</sup> Application for patent filed July 28, 1992.

1. As further explained on pages 5 through 8 of the specification (citations omitted, and footnote added):

Poly(organophosphazenes) are high molecular weight polymers containing a backbone of alternating phosphorous and nitrogen atoms. There are a wide variety . . . derived from the same precursor polymer, poly(dichlorophosphazene). The chlorine-substituted species can be modified by replacement of the chlorine atoms by different organic nucleophiles . . . The physical and chemical properties of the polymer can be altered by adding various ratios of hydrolytic sensitive side chains such as ethyl glycinate . . . This will affect the degradation of the polymer as an implantable and biodegradable material as well as vary the support of osteogenic cells for bone and tissue implants . . .

“[I]n order to maximize growth, increase cell attachment and promote permanent fixation by ingrowth of living tissue,”

[a] highly porous three-dimensional biodegradable [polyphosphazene] matrix with hydrolytically unstable side chains is prepared and used as a scaffold for the growth of osteoblast cells . . . the polyphosphazene includes between 10 and 90% hydrolytically unstable side chains including glucosyl, glycinyl, glyceryl, imidazolyl or ethoxy units . . . The addition of the glucosyl or glycinyl side chains to the polymer can also be used generally to enhance growth rates of cells adhered to the polymer, presumably through uptake and metabolism of the simple sugar or alcohol units.

As demonstrated by the examples, [polyphosphazene] substituted with 40% methylphenoxy and 60% ethyl glycinato side chains was fabricated into a porous three-dimensional matrix with an average pore density of 165  $\mu\text{m}$  using a salt removal technique.<sup>4</sup> Characterization by environmental scanning electron microscopy (ESEM) revealed an interconnecting porous network throughout the matrix with an even distribution of pores over the entire surface of the matrix . . . light microscopy revealed [osteoblast] cells growing

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<sup>4</sup> According to page 14 of the specification, “[a] particulate leaching process is used to create a porous polymeric matrix . . . particles are suspended in a polymer solution, the polymer solvent is removed, and the particles are leached out of the hardened polymer.”

within the pores as well as the surface of the matrix as early as the first day after seeding.

The claims are directed to biodegradable polyphosphazene matrices of defined porosity, i.e., with pore dimensions of between 100 and 250 microns, and methods “for repair or replacement of bone,” but are not limited to three dimensional structures. There are three rejections of the claims under 35 U.S.C. § 103; in our view the dispositive issue in each is the examiner’s proposed combination of Elia and Laurencin, so we shall consider the rejections together.

Elia is directed to methods, devices and materials for bone augmentation. “The bone augmentation material preferably is such that it hardens and sets over time and, as is the case with hydroxyapatite, . . . becomes attached to the existing bone structure because the bone structure grows into or around the bone augmentation material.” Column 11, lines 21-26. A containment system, or pocket, “inserted between facial tissue and underlying bone,” “is shaped to receive bone augmenting material and store [it] adjacent the underlying bone” until it hardens. Column 4, lines 4-11. “Further, the containment pocket [] is preferably formed of . . . material that is dissolved and/or resorbed by the body such that after a suitable period of time all that remains is the bone augmentation material.” Column 11, lines 26-30. Finally, the containment pocket may function as a porous barrier, “to control the flow of matter and/or energy in a deliberate way,” and “to contain and enhance the delivery of nutrients and other components that enhance the tissue reconstruction process.” Column 13, lines 3-14. In addition to materials like collagen, cross-linked

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proteins and gels, “polymers usable in a pocket or other containment structures . . . include, without limitation, poly(Amides), poly(Esters), poly(Orthoesters), poly(Anhydrides), poly(Ureas), poly(ALkyl 2-Cyancrylates), poly(Dihydropyrans), poly(Acetals), poly(Phosphazenes), and poly(Dioxinones).” Column 13, lines 34-40.

Laurencin teaches that polyphosphazenes, with the hydrolytically unstable side chains required by the claims, “are a class of bioerodible polymers whose use has only been explored for a limited number of biomedical applications . . . [primarily] in the area of controlled drug delivery and as material for encapsulation applications.” Pages 969-970 (citations omitted). As a “first step[] toward . . . the construction of an osteoblast-biodegradable polymer composite for skeletal regeneration,” “[a]n in vitro tissue culture model was chosen to investigate the potential of [polyphosphazene] to support osteoblast growth” and “provide a greater understanding of how the nature of polymeric surfaces influences cell attachment and growth.” Page 964. Cells were grown on polyphosphazene discs of various compositions, and Laurencin concluded that “osteoblast cell adhesion and growth can be modulated on [polyphosphazene] systems by varying the nature of the hydrolytically unstable side chain . . . [f]urther, the degradation rate of the polymer appears to be governed by the nature of the side chain . . . [t]hus, polyphosphazenes represent a system whereby modulation of cell growth and polymer degradation can occur simultaneously.” There is no indication that Laurencin’s hydrolytically unstable polyphosphazene polymers are processed to form pores of any size.

According to the examiner, Elia “meets the claim language except for the type of poly(phosphazene) as claimed . . . [h]owever, [Laurencin] teaches that the claimed phosphazene has been known to the art as a skeletal tissue regeneration material.” The examiner concludes that “it would have been obvious to use the polyphosphazene material of [Laurencin] . . . as the polyphosphazene material of [Elia] in order to promote ingrowth and in order to bring the controllable set of properties of hydrolytic stability and bioacceptability to the [Elia] invention.” Examiner’s Answer, page 4.

Appellants argue essentially that “[t]he device of Elia is a container to put bone material in,” e.g., hydroxyapatite, while Laurencin merely “discloses osteoblast-like cell growth on non-porous two-dimensional erodible systems.”<sup>5</sup> In contrast, “the claimed composition is a biodegradable matrix which serves as a temporary scaffold for the regeneration of skeletal tissue . . . formed from a polyphosphazene polymer which has been processed to form pores which the cells can migrate into and proliferate within,” in other words, “the claimed porous structure allows for sufficient space to promote cell fixation and growth,” enabling “bone actually to be replaced in whole or in part as opposed to merely providing a surface for growth or containment.” If we understand appellants’ argument correctly, it is that, unlike the situation in Elia, osteoblasts actually invade the

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<sup>5</sup> The examiner does not address the issue of porosity in the statement of the rejection, except to cite column 13 of Elia. In responding to appellants’ arguments regarding the porosity of the claimed devices, the examiner concedes that Laurencin does not disclose a porous polyphosphazene polymer, and again cites column 13, specifically lines 35-63, of Elia (which mentions a pore sizes of 25 to 400 microns). Examiner’s Answer, pages 4, 6 and 7.

claimed porous polyphosphazene structure, replacing the structure with bone as the polyphosphazene degrades. Brief, section V.

In our view, the mere fact that Elia's porous, biodegradable polyphosphazene matrix forms a temporary container, or pocket, for a "bone augmenting" substance, rather than forming the bone augmenting substance itself, does not distinguish it from the claimed matrix. Both Elia's container and the claimed polyphosphazene matrix are porous, biodegradable structures implanted at a site "for repair or replacement of bone." Nevertheless, Elia does not disclose the particular polyphosphazene derivatives, or narrow range of porosity, required by the claims. Thus, the ultimate issue raised by the examiner's rejection is whether the prior art provides a reason or suggestion which would have reasonably directed one skilled in the art to the claimed invention: a porous biodegradable structure, made up of the same polyphosphazene derivatives disclosed by Laurencin, "with pore dimensions of between 100 and 250 microns".<sup>6</sup>

Returning to Elia's disclosure, we note that there is no indication that the porous containment system functions as a growth surface for osteoblasts. Indeed, its purpose is to hold hydroxyapatite or a similar "bone regeneration material" against existing bone, and to control the passage of nutrients and other substances into and out of the bone

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<sup>6</sup> As stated in Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc., 75 F.3d 1568, 1573, 37 USPQ2d 1626, 1629 (Fed. Cir. 1996) (citation omitted), "It is well-established that before a conclusion of obviousness may be made based on a combination of references, there must have been a reason, suggestion, or motivation to lead an inventor to combine those references."

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regeneration material, until the bone regeneration material hardens and attaches to the existing bone. On the other hand, according to Laurencin, the “specific function” of hydrolytically unstable polyphosphazenes in bone repair “would be to support osteoblast growth, forming a bone-polymer matrix” (page 963). Thus, both Elia and Laurencin discuss the use of polyphosphazenes in the context of bone repair or replacement, but the specific function of Elia’s porous containment systems is entirely different from that of Laurencin’s hydrolytically unstable polyphosphazene growth supports.

Neither of the additional references cited by the examiner (Schacht and Lee) does anything to remedy the underlying deficiency in the examiner’s proposed combination of Elia and Laurencin.

We have no doubt that the prior art could be modified in the manner proposed by the examiner, but the fact that the prior art could be so modified would not have made the modification obvious unless the prior art suggested the desirability of the modification. In re Gordon, 733 F.2d 900, 902, 221 USPQ 1125, 1127 (Fed. Cir. 1984). Here, we find no reason stemming from the prior art which would have led a person having ordinary skill in the art to fabricate a hydrolytically unstable polyphosphazene matrix for repair or replacement of bone with the specific porosity required by the claims. In our judgment, the only reason or suggestion to combine the references in the manner proposed by the examiner comes from appellant’s specification.

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Accordingly, we reverse the rejections of claims 1 through 4 and 10 through 13  
under 35 U.S.C. § 103.

REVERSED

	)	
Douglas W. Robinson	)	
Administrative Patent Judge	)	
	)	
	)	
	)	BOARD OF PATENT
Carol A. Spiegel	)	
Administrative Patent Judge	)	APPEALS AND
	)	
	)	INTERFERENCES
	)	
Toni R. Scheiner	)	
Administrative Patent Judge	)	

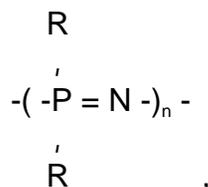
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APPENDIX

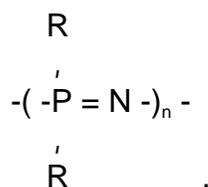
1. A polymeric matrix for repair or replacement of bone formed of a biodegradable, biocompatible polyphosphazene formed from the repeat unit



wherein R is a side chain selected from the group consisting of aliphatic, aryl, aralkyl, alkaryl, carboxylic acid, heteroaromatic, carbohydrates, heteroalkyl, halogen, (aliphatic)amino, heteroaralkyl, di(aliphatic)amino, arylamino, diarylamino, alkylaryl amino, oxyaryl, oxyaliphatic, oxyalkaryl, oxyaralkyl, thioaryl, thioaliphatic, NHC(O)O-(aryl or aliphatic), -O-[(CH<sub>2</sub>)<sub>x</sub>O]<sub>y</sub>-CH<sub>2</sub>)<sub>x</sub>NH<sub>2</sub>, -O-[(CH<sub>2</sub>)<sub>x</sub>O]<sub>y</sub>-CH<sub>2</sub>)<sub>x</sub>NH(CH<sub>2</sub>)<sub>x</sub>SO<sub>3</sub>H, and -O-[(CH<sub>2</sub>)<sub>x</sub>O]<sub>y</sub>-(aryl or aliphatic), wherein x is 1-8 and y is an integer of 1 to 20,

wherein the matrix is a porous structure with pore dimensions of between 100 and 250 microns.

10. A method for repair or replacement of bone comprising implanting at a site in need of repair or replacement a polymeric matrix formed of a biodegradable, biocompatible polyphosphazene formed from the repeat unit



wherein R is a side chain selected from the group consisting of aliphatic, aryl, aralkyl, alkaryl, carboxylic acid, heteroaromatic, carbohydrates, heteroalkyl, halogen, (aliphatic)amino, heteroaralkyl, di(aliphatic)amino, arylamino, diarylamino, alkylaryl amino, oxyaryl, oxyaliphatic, oxyalkaryl, oxyaralkyl, thioaryl, thioaliphatic, NHC(O)O-(aryl or aliphatic), -O-[(CH<sub>2</sub>)<sub>x</sub>O]<sub>y</sub>-CH<sub>2</sub>)<sub>x</sub>NH<sub>2</sub>, -O-[(CH<sub>2</sub>)<sub>x</sub>O]<sub>y</sub>-CH<sub>2</sub>)<sub>x</sub>NH(CH<sub>2</sub>)<sub>x</sub>SO<sub>3</sub>H, and -O-[(CH<sub>2</sub>)<sub>x</sub>O]<sub>y</sub>-(aryl or aliphatic), wherein x is 1-8 and y is an integer of 1 to 20,

wherein the matrix is a porous structure with pore dimensions of between 100 and 250 microns.