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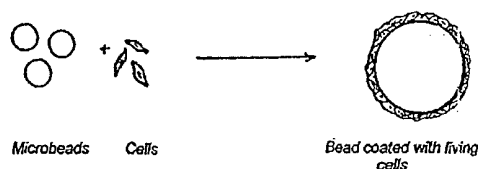
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- Published: — with international search report

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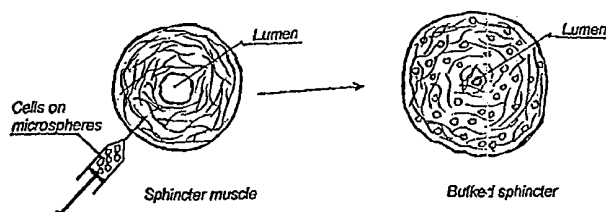
(54) Title: INJECTABLE MICROSPHERES FOR DERMAL AUGMENTATION AND TISSUE BULKING

SCHEMATIC REPRESENTATION OF SPHINCTER BULKING

1. COATING OF MICROBEADS SURFACE WITH CELL IN VITRO



2. SPHINCTER BULKING



Beads are first coated with cells *in vitro*.

Coated beads are then injected in physiological conditions inside the sphincter. The sphincter volume increases proportionally to the amount of injected beads and the lumen size decreases. Beads are progressively and non reversibly integrated within the muscles.

(57) Abstract: The present invention relates to elastic, hydrophilic and substantially spherical microspheres useful for dermal augmentation and tissue bulking. The invention provides injectable compositions comprising the microspheres and a biocompatible carrier for use in dermal augmentation. The present invention further provides methods of dermal augmentation and tissue bulking, particularly for the treatment of skin contour deficiencies, Gastro-esophageal reflux disease, urinary incontinence, and urinary reflux disease, using the injectable compositions.



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— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

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**INTERNATIONAL SEARCH REPORT**

International Application No

PCT/US 01/08529

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC 7 A61L27/38 A61L27/60 A61L27/54 A61L31/00 A61L31/16

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 7 A61L A61K C12N

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 practical, search terms used)

WPI Data, EPO-Internal, PAJ, BIOSIS, COMPENDEX, CHEM ABS Data, EMBASE, MEDLINE

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 44643 A (BIOSEPPRA INC) 10 September 1999 (1999-09-10) page 4, line 24 -page 5, line 2 page 7, line 24 -page 8, line 2 page 12, line 3 - line 30 examples claims	1-44
A	WO 96 12510 A (DIMOUDIS NIKOLAOS ;HARTINGER ANTON (DE); BOEHRINGER MANNHEIM GMBH) 2 May 1996 (1996-05-02) claims	1-44
A	WO 92 06702 A (UNIV NEW YORK) 30 April 1992 (1992-04-30) page 6, line 18 -page 7, line 22	1-44
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Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
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- \*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
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- \*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.
- \*Z\* document member of the same patent family

Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

International Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>LAURENT ALEXANDRE ET AL: "Trisacryl gelatin microspheres for therapeutic embolization, I: Development and in vitro evaluation."                      AJNR,                      vol. 17, no. 3, 1996, pages 533-540,                      XP001031867                      ISSN: 0195-6108                      the whole document</p> <p style="text-align: center;">---</p>	
A	<p>BEAUJEU Remy ET AL: "Trisacryl gelatin microspheres for therapeutic embolization, II: Preliminary clinical evaluation in tumors and arteriovenous malformations."                      AJNR,                      vol. 17, no. 3, 1996, pages 541-548,                      XP001031874                      ISSN: 0195-6108                      abstract                      page 541, right-hand column, paragraph 2</p> <p style="text-align: center;">-----</p>	

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/08529

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9944643	A	10-09-1999	AU 2891699 A 20-09-1999
			CN 1299291 T 13-06-2001
			EP 1059943 A1 20-12-2000
			WO 9944643 A1 10-09-1999
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WO 9612510	A	02-05-1996	DE 4438015 A1 02-05-1996
			AU 3806695 A 15-05-1996
			WO 9612510 A1 02-05-1996
			EP 0788381 A1 13-08-1997
			JP 9511673 T 25-11-1997
			US 5980888 A 09-11-1999
			ZA 9508982 A 24-04-1997
-----			
WO 9206702	A	30-04-1992	AU 665933 B2 25-01-1996
			AU 8923591 A 20-05-1992
			CA 2094280 A1 20-04-1992
			EP 0554352 A1 11-08-1993
			JP 6502406 T 17-03-1994
			WO 9206702 A1 30-04-1992
			US 5618531 A 08-04-1997
			US 5750103 A 12-05-1998
			US 6060048 A 09-05-2000
			US 6264943 B1 24-07-2001
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