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REVIEW

A review of biovitroceramic PAW1 – Romanian bioactive implant material for ossiculoplasty

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Abstract: *A successful ossiculoplasty (reconstruction of the ossicular chain of the middle ear), even now, almost a hundred years after the first attempts and countless tested materials, remains a challenge through the complexity of the surgical act and through the repeated attempts to find the most adequate prosthesis to re-establish, in the long term, the sound conductive mechanism.*

In this article, we present a review of the main implanted materials, including the biotechnological aspects of ossicular chain reconstruction with an emphasis on the Romanian contribution to this field of study.

Keywords: *prostheses, implants, ossiculoplasty, ceramics, ossicular chain, biotechnology, biocompatibility, biovitroceramic PAW1*

INTRODUCTION

Ossiculoplasty is a surgical procedure used to restore hearing loss by reconstructing the ossicular chain mechanism between the tympanic membrane and the oval window, in the presence of a discontinuity or fixation, with or without a concomitant disease. The medium-term and especially the long-term success of this intervention depends on several important factors: the skill of the surgeon, the material used in the reconstruction of the ossicular chain, and, most importantly, a preserved, quality middle ear.

Chronic suppurative otitis media (COM), with or without cholesteatoma [1], is the most common pathology that influences the outcome of surgery and the long-term functional and anatomic results. The functional results become even more important if you consider that hearing loss of variable etiology represents one of the most challenging public health issues confronting the world's population [2]. "The integrity of the auditory system is one of the prerequisites for the acquisition and the proper development of oral language and a person suffering from hypoacusis is more likely to have poorer professional results than his colleagues, and will be less competitive in the labor market, and will have smaller chances to complete higher education" [3,4].

The next most important factor influencing results is the type and the quality of the material. Over time many types of materials have been tested (biological and synthetic), some entering into medical practice a shorter period, others remaining in current use, but the surgeon's choice for the ossicular chain reconstructions depends on their own experience in the field, the ossicular deficiency or the patient's immunological status [5]. The purpose of all these attempts is to implant a type of material with excellent biocompatibility, and stability, to provide natural sound transmission with the minimum risk of potential bacterial colonization or graft rejection [6].

THEORY AND CONCEPT

Ossicular substitution or reconstruction has been attempted with an array of materials but the only conclusion that has been drawn is that "the ideal prosthesis for ossicular reconstruction should be made of a material that maintains

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its shape, rigidity, and acoustic properties, as well as being cost-effective. This material should also be biocompatible, safe, and easily inserted and modified" [7].

From the acoustical point of view, a prosthesis is well designed, if its shape and material reach a high stiffness combined with a low mass but is also small, relatively cheap, and easy to modify [8,9,10,11].

From this point of view, titanium has advantages compared with gold, ceramics, or plastics because of its low density and high mechanical strength. These properties of titanium significantly reduce possible loss in sound transfer due to internal resonances. The higher mass of gold and ceramic prostheses decreases the motion of the entire system above the first resonance.

This inertia influence can also be seen by a decrease in the first resonance frequency of the (reconstructed) middle ear system. "By contrast, the low mass of the light titanium prostheses contributes to a better sound transfer performance, especially in the high-frequency range." [12]

A further significant parameter is the quality of prosthesis coupling to both tympanic membrane/malleus and stapes. The dynamics of the reconstructed middle ear are very sensitive to where and how the prosthesis is coupled to the tympanic membrane and ossicles, to the spatial direction in which the prosthesis is oriented, and to the prosthesis attachment (near rigid or rather loose attachment). In a patient, the prosthesis attachment may be influenced by the resulting tension that is achieved both by the surgeon and by postoperative wound healing.

Prosthesis placement is paramount for obtaining good functional results, but this represents no guarantee that postoperative migration relative to the malleus handle, TM, or stapes will not occur [13,14]. This is highly dependent on the skill of the surgeon; the type of prosthesis and we should never forget that medical research can sometimes require a high degree of abstraction and theorization [15].

"Ossicular reconstruction materials are categorized as autografts, homografts, and alloplastic prosthetics. Each of these materials has advantages and disadvantages for use in the middle ear" [7].

BIOLOGICAL MATERIALS

Hall and Rytzner (1957) performed the first chain reconstruction using autogenous incus [16]. Several otologists, including Farrion, Sheehy, and Guilford, began reporting on the success of using autografts for ossicular reconstruction, especially for the body of the incus [17]. However, the patient's incus is not always available for repositioning and Farrion first advocated the use of cortical bone as an ossicular substitute [17,18].

As a biological alternative to ossicles, cartilage has been extensively used in tympanoplasty and ossiculoplasty [18]. Autologous tragal and/or conchal cartilage is, however, not always suitable for ossicular chain reconstruction, especially in cases where the stapes arch is missing since they do not have the required mass, stiffness, and thickness [19]. Zini et al. (1984) introduced ossicular prostheses made from costal cartilage and reported no extrusion at 10 years of follow-up with stable functional results over the years [19].

Autologous materials presented a high degree of tolerance within the middle ear and provided reliable hearing results. Their disadvantages were the laborious and time-consuming sculpting into the required shape and the scarceness of material in chronically diseased ears [4] loss of rigidity (especially with cartilage), and possible fixation to the soft tissues of the middle ear [17].

Homografts (as an option for unreliable autografts) were first used for middle ear reconstruction in 1966 by House and colleagues and later led to the use of "irradiated ossicles, cartilage, and even homograft tympanic membranes with en bloc ossicles" [20,21]. The hearing results and biocompatibility of homografts and autografts proved similar but the risk of disease transmission of HIV and prions (i.e., Creutzfeldt-Jakob disease) brought their decline in use – see Table 1.

Donor (D) – Receiver (R) Relationship:
1. Autologous: D ≡ R
2. Isologous: D·R Homozygotic Twins
3. Homologous (Alloplastic): D·R Same species
4. Heterologous (Xenoplastic): D·R Different species

Donor Situs (D.S.) to Receiving (R.S.) situs Relationship:
1. Orthotopic (same situs): D.S. ≡ R.S.
2. Heterotopic (different situs): D.S. ≠ R.S.

Although many surgeons preferred biological prostheses due to increased compatibility with the middle ear and low rate of rejection, the lack of materials and prolonged intraoperative time led the researchers to look for the ideal material in the reconstruction of sound conducting mechanisms.

SYNTHETIC MATERIALS

Other than the natural or biological materials (autologous and homologous), polymers, ceramics, and metals are currently used for ossicular chain reconstruction, each with its advantages and disadvantages. These synthetic materials are defined as biomaterials.

In 1958, Shea used for the first-time polyethylene prostheses (Polytef – Teflon and silicone elastomer – Silastic) for middle ear reconstruction [17] with excellent short-term hearing results. The high extrusion rate, significant middle ear reactivity towards synthetic materials, and risk of penetration into the inner ear [17] caused this material to gradually drop out of use.

Table 1: Types of natural biomaterials used in ossiculoplasty

Natural Biomaterials (Grafts, Transplants)				
Type	**Status**	**Donor–Receiver Relationship**	**Species**	**Author, Year**
Autologous	Fresh	Orthotopic	Remodeled malleus	Wullstein, 1953
		Heterotopic	Cartilage Tragal cartilage Septal cartilage Rib cartilage Mastoid cortical bone	Williams, 1958 Utech, 1960 Jansen, 1962
Homologous (Allo)	Preserved	Orthotopic	Isolated ossicles Ossicular chain	Portmann, 1959 Marquet, 1966
		Heterotopic	Mastoid cortical bone Septal cartilage Rib cartilage Meniscus cartilage Dentine	Wullstein, 1952 Jansen, 1960 Zini, 1967
Heterologous (Xeno)	Preserved	Orthotopic	Veal incus	Sultan, 1983
		Heterotopic	Veal rib cartilage	Zini, 1959
	Normal	Normal	Coral	Robier, 1987 Schmorll, 1990

After almost 20 years of research, in 1976, Shea reported on the use of a high-density polyethylene sponge (Plastipore), a porous, nonreactive material that could allow the in-growth of tissue [22]. "A similar thermal-fused porous polyethylene (Polycell) was developed later and allowed the prosthesis to be coupled to other materials, such as stainless steel thus enabling various prosthesis designs" [17]. The most-reported problem of such porous materials was the high extrusion rate when in direct contact with the TM. However, a disc of cartilage placed between the head of the prosthesis and the tympanic membrane gives excellent long-term results even today [22,23].

In 1979 the era of ceramics in ossicular reconstruction begins by introducing a few categories of alloplastic materials, either bioinert or bioactive. Implantable materials that do not release detectable trace substances are termed bioinert. The prototype bioinert material is dense aluminum oxide ceramic (Al_2O_3), popular in Germany and Japan in the 1970s. The implant can be fitted to the under-surface of the tympanic membrane without cartilage coverage [24].

By studying the way, the body reacts to the implanted materials, there can be three major recipients defined (Tables 2, 3, 4):

● "bioinert" – the body does not react to the implant material.

● "bio-tolerated" – the local tissue regards the implant as a foreign body but does not react, the material is not excluded.

● "bioactive" – the local tissue reacts and tends to create a stable bound to integrate it [6].

"Bioactive implants, such as glass-ceramic (Ceravital), were biocompatible and reacted with surrounding soft tissue and adjacent bone allowing a coupling between the implant and the ossicle" [19,25] and were used, with various results, around the world, even in the former communist bloc, including Romania [26].

Hydroxyapatite, found in the mineral matrix of living bone, was introduced for tympanoplasty surgery in 1984 by Grote (calcium phosphate ceramic) [27]. It is a bioactive material that can be easily integrated into surrounding tissues (bone). The first results by Wehrs et al. reported functional success and a low extrusion rate 4 years after implanting hydroxyapatite incus or incus/stapes prosthesis. Since that time, this material has been adapted to various uses and prosthesis designs [17,20].

Titanium prostheses were developed and first used in Germany in 1993 and have been growing in popularity ever since. The material is rigid and biocompatible just like

hydroxyapatite, but much lighter. It is also nonmagnetic and allows it to be manufactured in many precise shapes. "Most of the titanium prostheses possess an open head, allowing better visualization during placement" [17].

Table 2: Types of synthetic bioinert materials used in ossiculoplasty.

Name	Composition, Chemical structure, Family, Order	Author, Year
ALUMINA FRIALIT CORINDON	Al_2O_3 Oxide Ceramics	Plester & Jahnke, 1979
BIOCERAM	Al_2O_3 Y_2O_3	Yammamoto & Ywanaga, 1983
MACOR CERAMIC	Fluor phlogopite mica-Borosilicate glass $SiO_2 \cdot MgO \cdot Al_2O_3 \cdot K_2O \cdot B_2O_3 \cdot F$	Pauler & Jahnke, 1984
VITROCARBON	Glass - Carbone	Blemke et al. 1987

Table 3: Types of synthetic bioactive materials used in ossiculoplasty.

Name	Composition, Chemical structure, Family, Order	Author, Year
BIOGLASS 45-S-5	Silicon-Phosphorus Bio-glass $SiO_2 \cdot CaO \cdot Na_2O \cdot P_2O_5$	Hench et al., 1970
CERAVITAL	Silicon-Phosphorus Bio-vitro-ceramic (Hydroxyapatite – Glass) $Li_2O \cdot ZnO \cdot SiO_2$	Brömer et al., 1973
CERABONE A-W	Hydroxyapatite – Glass- β-Wollastonite ($CaO \cdot SiO_2$)	Kokubo et al., 1982
IMPLANT L-I	Hydroxyapatite – Glass- β-Wollastonite ($CaO \cdot SiO_2$)	
BIOVERIT I	Mica – Apatite – Glass $SiO_2 \cdot (Al_2O_3) \cdot MgO \cdot Na_2O \cdot K_2O \cdot F \cdot KO \cdot P_2O_5$	Holland &Vogel, 1987
BIOVERIT II	Mica – Glass – Corderite	Holland & Vogel, 1993
BIOVITROCERAMICS PAW-1	Fluro-hydroxyapatite – Wollastonite – Glass $B_2O_3Fl_2$	Rădulescu & Negreanu, 1993

Table 4: Types of synthetic bio-tolerated materials used in ossiculoplasty.

Name	Composition, Chemical structure, Family, Order	Author, Year
PALAVIT	Vinyl-acrylic resin	Wullstein, 1952
SUPRAMID	Polyamide (Nylon)	Kley, 1955
POLYETHYLENE	Non-porous, low-density polyethylene	House, 1960
TEFLON	Polytetrafluoroethylene (C2F4)n (PTFE)	Shea, 1962
NON-OXIDATIVE STEEL TANTALUM SILVER ZIRCONIUM TITANIUM	Non-oxidative metals	Schucknecht, 1971
PROPLAST	Polytetrafluoroethylene (TEFLON) – Carbon fibre composite	Shea, 1974
PLASTIPORE	High-density polyethylene sponge (HDSP)	Shea, 1974
POLYCEL	Thermal fused HDSP	Fisch, 1981

Classification of Synthetic Biomaterials:

1. Destination:
   1.1. Tissue
   1.2. Organ
   1.3. Function
2. Composition:
   2.1. Monocomponent
   2.2. Policomponent
3. Structure – Mass - Form:
   3.1. Monostructure
   3.2. Polistructure
4. Relationship to Host (Recipient):
   4.1. Biotolerated
   4.2. Bioinert
   4.3. Bioreactive (Active, Bio-reactive, Bioactive)
   4.4. Composite (e.g., Tolerate + Active)

BIOVITROCERAMIC PAW-1 AND THE ROMANIAN CONTRIBUTION

Synthesized in 1990 by Dr. Ing. Popescu-Negreanu, PAW-1 was tested physically, chemically, and biologically (in vitro and in vivo) between 1991 and 1992 and homologated on March 31st, 1993.

Bio-vitro-ceramic PAW 1 is a solid, bio-reactive material, made up of fluoro-hydroxyapatite and wollastonite microcrystals encompassed into a vitreous mass (glass). Hydroxyapatite, which is the mineral matrix of living bone, is a well-tolerated osteoinductive material that does not produce necrotic phenomena in adjacent tissues and does not give foreign body reactions [26] – see Table 5.

Table 5: Taxonomy of PAW1.

General Taxonomy of PAW1
Class: Solids with biphasic structure (crystalline and non-crystalline) **Order**: Ceramics **Family**: Bio-vitro-ceramics **Genus**: Silicon – Phosphorus **Species**: Controlled porosity **Variety**: α - closed porosity (dense) β– opened porosity (porous)
Special Taxonomy of PAW1
Synthetic **Destination**: Organ **Composition**: Poli-component **Structure – Mass – Form**: Monostructure **Relationship to Host (Recipient)**: Bioactive

Medical use:

1. Dentistry: Central Military Hospital, Bucharest since June 1993
- Parodontopathy
- Granules

2. Oral and maxillofacial surgery/Esthetics: Prof. Burlibașa, Prof. Gănuță since 1993
- Granules
- Shaped implants

3. Orthopedics: Central Military Hospital, Bucharest and Foișor Orthopedics Hospital, Bucharest, Prof. Popescu Mihai since 1993
- Granules
- Shaped implants

4. Neurosurgery: "Bagdasar-Arseni" Neurosurgical Hospital, Bucharest, Prof. Dănăilă since 1994
- Shaped implants

5. Otorhinolaryngology (Otology): IFACF-ORL Prof. Dorin Hociota, Dr. Marian Rădulescu since June 1993
- Ossicular chain implants (PORP, TORP)

Chemical composition:
1. Fluorohydroxyapatite: $[Ca_{10}(PO_4)_6(OH)xFl_2\text{-}x]$
2. β-Wollastonite ($CaO \cdot SiO_2$)
3. Boron trioxide: B_2O_3
4. Fluoride: Fl_2

The material is obtained by thermally controlled crystallization (ceramization) of glass from the Silicium-Calcium-Magnesium-Phosphorus system ($SiO_2 \cdot CaO \cdot MgO \cdot P_2O_5$) with minute additions of Borum trioxide (B_2O_3) and molecular Fluoride.

Biological properties:

1. Biocompatibility:
- Predictive: Good, due to the identity of the crystalline phase of the material to the mineral phase of the mature bone.
- Experimental: tested through the low rejection rate of middle-ear implants.

2. Biodegradation:
- Predictive: Null without inflammation/infection. Osteogenesis on the implant-tissue interface.

Identical to the bone with inflammation/infection.
- Experimental: Clinical – the study of rejected implants degradation

Paraclinical – Rx for integrated implants/HP for rejected.

3. Bioactivity:
- Predictive: Good, based on the physical and chemical structure.

Porosity – cell colonization and mechanical anchorage.
Chemical structure: Chemical anchorage (direct) = covalent ties at the implant-tissue interface. Osteogenesis on the interface.
- Experimental: tested through the rate of histological integration and rate of tympanic membrane perforation.

4. Bio-functionality:
- Predictive: Good, based on mechanical and vibro-mechanical properties.
- Experimental: tested through therapeutic efficiency (audiological gain – dB): Air-bone Gap (ABG) pre-operatively vs. post-operatively.

CONCLUSION

Although numerous techniques and materials have been used for ossicular reconstruction, the quest for the ideal prosthesis and the best-suited materials is ongoing. This research took place all over the world during the past century and even developing countries such as Romania played a role.

The autochthonous bio-vitro-ceramic PAW1 proved to be a reliable, resilient material with a high degree of

biocompatibility and good functional results.

The best combination of biocompatibility, toughness, ease of shaping, and inserting are still to be found.

Today, autogenous, and alloplastic prostheses are equally used with good outcomes, but the final decision remains to the surgeon, and it would be wise that he chooses the one that is most comfortable for him and provides consistent and favorable results.

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Authors' contribution
Conceptualization: RM, AIM. Data curation: AIM, RM. Formal analysis: AIM, RM. Methodology: RM. Project administration: AIM. Visualization: AIM. Writing - original draft: AIM, RM. Writing - review & editing: RM, AIM. All authors read and approved the final manuscript.

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The present work represents a review of the literature and therefore requires no agreement from the Research Ethics Committee.

Patient consent for publication
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