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Polyimide MP-1™- The Ultimate Solution for Medical Devices

Alisa Buchman, Simha Sibony

MMATECH Ltd., P.O.Box 12082, Nahariya, Israel

Abstract: *MMATECH Ltd. introduced into the medical device market the game changing polymeric material, MP-1™, a derivative of the polyimide family. The use of metals in orthopedics involves increasing concern of developing pre-cancerous tumors in tissues and hyper-sensitivity reactions to metal debris of implant devices. As such, MMATECH was developing a new polymeric substitute, MP-1™, for implant devices. A comprehensive pre-clinical research, which included biological, chemical, mechanical and physical tests, was conducted. The pre-clinical tests showed excellent biocompatibility, no wear, self-lubrication, high durability and safety of the MP-1™ material. Following these results, the first articulating implant, a hip acetabular liner, was developed and clinically implanted. Due to constant increase in human life expectancy, more people require primary and revision total hip replacement surgeries, costing billions of US$ per year. More than 115 MP-1™ Acetabular liners are already implanted with 2-15 years Follow-up, as part of THR clinical study with excellent results. Femoral ball is the next device made of MP-1™, being tested as an additional part of THR implant. A new family of MP-1™ devices was developed for trauma injuries funded by the EU Horizon 2020 project. Orthopedic fractures are a common daily acute health issue. A significant increase of bone fracture is expected in the coming years due to aging population, more active lifestyle, falling, and road and sport injuries. Fractured bone injuries are normally treated using various fixation implants (nails, screws and plates) made of metal or composite materials. The newly developed MP-1™ trauma implants have the advantage of being a non-metal device which is easier and quicker to implant and safer to use. Three kinds of trauma devices were developed – a proximal Humerus nail, a proximal plate and a distal radius screw. All three devices were pre-clinically tested and clinically implanted in animals. Histology results showed excellent biocompatibility with growth of new bone around the implant within 6 weeks. MP-1™ has other advantages such as being radio-opaque, delaying blood clotting and avoiding growth of biofilm. All these features promise interesting applications and a wide range of development in future medical devices.*

Introduction

While the orthopedic device industry is changing its trend from metals devices into polymers over the last two decades, the push for new substituting material innovation has inclined. Entering a new decade, of polymer innovation in orthopedics, provides greater design freedom and higher long lasting compatibility with the body at a significant lower production price. While trends can differ by application, the promising characteristics that emerge create polymers that are more flexible, strong, biocompatible, safe and cost-effective than the last generation. Another area of controversy is metal hypersensitivity, a delayed immune response thought to occur when a patient receives an orthopedic implant that contains a type of metal to which they are sensitive or allergic. In literature reports, about 10% of the general population were found to have metal hypersensitivity to nickel, cobalt, chromium or molybdenum [1]. Using polymers as substitute to metals will solve this issue.

Due to constant increase in human life expectancy, more people require primary and revision total hip replacement surgeries, costing billions of US$ per year. Currently used ceramic on X-linked Polyethylene appears to be the best choice by default, but it still wears. Metal on Metal (MoM) has been abandoned due to metal ion release and Pseudo-tumor production. Ceramic on ceramic can squeak and is intolerant of malposition that results in high friction, stripe wear and micro-fractures. The wear particles generated of bearing systems, are the major cause of osteolysis and joint failure. During 2011-14, leading orthopedic companies suffered global recalls of their MoM hip systems resulting in thousands of revision surgeries [1-5]. The search continues for new and more durable materials bearing materials. Developments in medical technology have increased the demand for advanced materials and their use in various applications in the medical industry. Key drivers for increased demand for medical devices include growing and aging population, advanced medical procedures and complicated/ contagious diseases. Metals and ceramics are prevalent in the medical industry. However, the unique properties of polymeric materials exhibit potential as better replacements for conventional materials. The goal therefore was to develop an alternative material for use in orthopedics that does not generate wear debris of a type that induces osteolysis. This article presents the alternative using the polymer polyimide (MP-1™) as a replacement for the conventional materials used in orthopedic application.

Preclinical results

MMATECH Ltd. has developed a new articulation liner made of a revolutionary material of the Polyimide family, MP-1™, a spin-off of the Aerospace industry (Fig. 1). MP-1™ has proved to be biocompatible, heat-

resistant, highly crosslinked, combining unusual strength, toughness, self-lubrication, excellent friction and wear durability, as well as resistance to fatigue, creep, impacts and chemicals. These properties lead to longer life span and safer articulating implanted components.

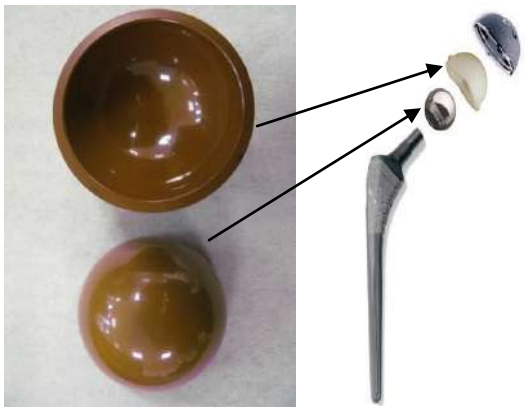

Fig. 1: *Acetabulat liner and femoral head made of MP-1™*

Traditional metallic implants can result in a phenomenon called "stress shielding". Stress shielding occurs when a stiff metallic implant tends to carry the majority of the load rather than the preferred load sharing where the bone and the implant share the load carrying duties. When the metallic implant carries the majority of the load, the adjacent bone weakens over time. To achieve the desired load sharing for structural orthopedic implants, it is critical to use an implant material with similar modulus of that bone. Cortical bone has a modulus of 14 GPa, Titanium implants have a modulus of 110 GPa and MP-1™ has a modulus of 3.7 GPa. Metallic, ceramic and Polyethylene articulating implants tend to release sub-micron wear particles from the surface, which tend to invade the tissues surrounding the implant causing poisoning and tumor growth [2-5]. Metallic articulating implants are thus scarcely in use anymore since the recall of De-Pue's hip implants in 2011. The wear debris of MP-1™ are all over 2 µm and thus can't be swallowed by macrophage and cause inflammation.

MMATECH Ltd. developed an advanced polyimide MP-1™ appeared to be the most promising solution. MP-1™ is a high temperature thermoset polymer, consisting of an aromatic backbone molecular chain, which is interconnected by ether functional groups. This chemical structure confers stability at very high temperatures (exceeding 400°C), resistance to chemicals and radiation damage, and durability to creep and fatigue (Table 1).

Table 1: *Mechanical results of MP-1™*

Property	*Test Method*	Units	**MP-1™ ***
Tensile Strength	ASTM D 638	MPa	**108**
Tensile Modulus MPa	ASTM D 638	MPa	**3748**
Tensile Elongation @ Break	ASTM D638	(%)	**8.9**
Impact Strength	ASTM D 256	Ft.Lb/Inch	**1.65**
Glass transition Tg	DSC, TMA	°C	**311**
Compr. Str. @10% Compr. Modulus Flexural Str. Flexural Modulus	ASTM D 695 ASTM D 695 ASTM D 790 ASTM D 790	MPa MPa MPa MPa	**164** **3900** **112** **4273**

The availability of poly-aromatic polymers arrived at a time when there was growing interest in the development of “wear free” hip acetabular liners and femoral balls, with stiffness comparable to bone [6]. The evolution of polyimide MP-1™ has been studied extensively for bio-medical applications resulting from excellent biocompatibility and mechanical properties. MP-1™ is the first generation of polyimides used in medical devices. The special chemical composition of the MP-1™ polyimide enables it to be used for long-term implants because of significant hydrolytic resistivity and long term durability. MP-1™ is totally inert and is not prone to oxidation or solvent's attack or any degradation. In articles [7,8] the pre-clinical testing of MP-1™ was described revealing the chemical, physical and mechanical properties of the material including creep and fatigue. A full series of biocompatibility tests was executed and described as well. The results have proved that MP-1™ is totally biocompatible, has better fracture toughness than ceramics, better wear resistance than polyethylene, minimal friction coefficient, it is self-lubricating, and has chemical inertness and high durability in fatigue and creep resulting in dimensional stability and high endurance limit.

MMATECH conducted specific tests aiming at articulating joints. These included Hip simulator, catastrophic impact test, stability tests and aging stability. All these tests proved the safety of the material before approaching clinical trials.

Hip simulator results after 5 million cycles in saline solution are shown in Fig. 2. Under these conditions, the MP-1™ exhibited an order of magnitude less wear than the UHMWPE control. Fluid analysis showed that the volume of particles from the MP-1™ material were significantly low (0.044 mm^3 after 5M cycles = 5 Years). The size of the MP-1™ particles generated from the hip simulator was 1.9 - 23 µm while the size of

UHMWPE particles was 0.694 µm and less (sub-micron). This explains why MP-1™ debris are totally compatible with the human body.

A test done on biocompatibility of MP-1™ wear debris in Rodent's body revealed an excellent compatibility (Fig. 3) showing the inertness of the MP-1™ particles in the surrounding tissue [9].

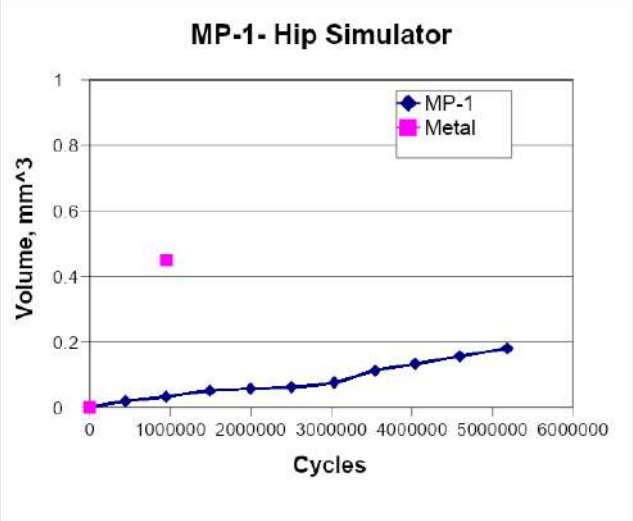

Fig. 2: *Hip simulator results of MP-1™ vs. Ceramic and metal vs. metal*

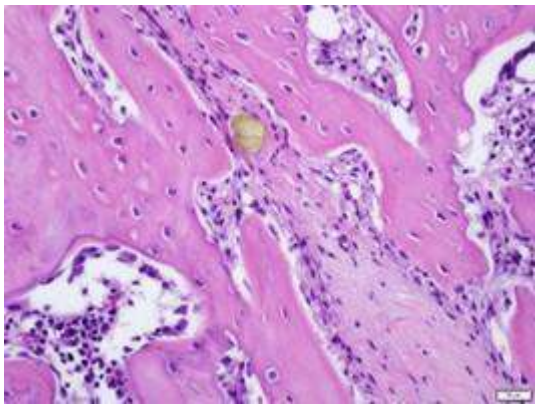

Fig. 3: *MP-1™ wear debris in tissue*

Catastrophic impact test proved that MP-1™ can withstand loads at the range of 10 times human body weight and hammering of the implant during surgery. Six cylinders of MP-1™, 2mm thick, were impacted 100 times with a load of 700 Kg. Results showed no visible damage and no failure of the parts. All six parts stayed intact proving the excellent impact resistance of MP-1™.

A new application produced from MP-1™ material are the trauma devices for fixation of fractures. MMATECH developed the MP-ORIF game changing Open Reduction Internal Fixation (MP-ORIF) implant to replace the currently used metal orthopedic implants in trauma surgery. MMATECH developed three kinds of devices: the proximal Humerus implant, proximal plates and distal radius screws made of MP-1™ [10]. Pre-clinical tests were conducted. The devices were tested under bending and flexure loads and performed excellent results. The screws were tested under pull-out forces.

Clinical study

Due to the excellent pre-clinical results of the MP-1™ material and acetabular liner device in hip simulator, lever out, push out, torsional stability and catastrophic impact as well as dimensional stability in a long time storage [8], an advanced clinical study was performed. The pre-clinical results proved that this family of polymers (polyimides) will be inherently strong, inert, and biocompatible, more than other currently used biomaterials that have been clinically tested for the last few decades.

In October 2011, MMATECH received the CE and ISO certificates for its MP-1™ Acetabular liner based on a pilot clinical study conducted in New Zealand with excellent 15y follow-up results. A retrieval study at 6.5y showed no reaction in the bone marrow, no osteolysis and minimal synovial response. There was no measureable MP-1™ liner wear or femoral ceramic ball wear.

Ethical Committee approval was granted for a clinical study on MP-1™ acetabular liner in THR of 100 patients with a single surgeon to be carried out in New Zealand, using an acetabular shell from an approved EU manufacturer. The results of the first 88 surgeries follow-up since January 2013 demonstrate normal blood parameters, no osteolysis, and improved quality of life, with Oxford Hip scores up to 48/48 (Fig. 4). The performance of MP-1™ even at 15 years is very promising and is now being applied to younger patients (~ 40 Y old) in view of the retrieval data. Helsinki Ethical Committee approved clinical studies on MP-1™ acetabular liner in THR in Israel. Two additional clinical studies in two different centers in Israel (Rambam RMC and Haemeq RMC) were conducted with 8 and 21 surgeries respectively. These trials began in Sep. 2017 and Oct. 2018 respectively. Follow-up of 1-2 years proved excellent results.

Moreover, with the replacement of material to MP-1™ in the overall set-up of total joint replacement the length of stay for THR changed from 2 weeks to 1-2 days mean for primary THR cases. This advantage has also an impact on reimbursement and financial expences.

Clinical study of the trauma devices was conducted in animals: rodents and sheep. Clinical study in humans will follow in three different centers.

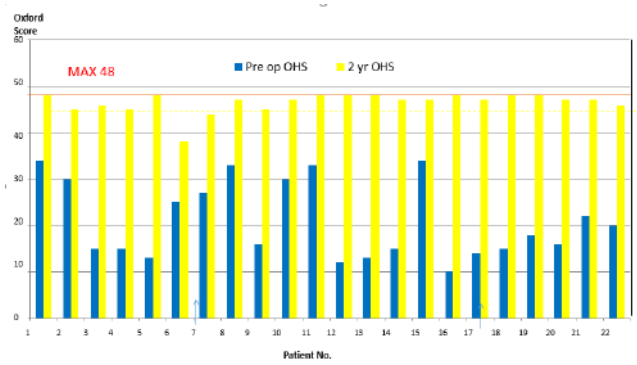

Fig 4: *Oxford score before operation compared to 2 years after operation*

Conclusion

Due to its high inertness, MP-1™ biomaterials is an attractive platform to develop many different novel bioactive devices. MP-1™ will be an alternative to metallic biomaterials in the orthopedic community for implantation and fracture fixation implants.

Acknowledgement

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References

[1] Susan M. Rapp, Metal allergy: A clinical conundrum, Orthopedics Today, Jan 2019

[2] Kurtz S. M, Muratoglu O.K, Evans M, Edidin A.A., Advances in the processing, sterilization, and crosslinking of ultra-high molecular weight polyethylene for total joint arthroplasty, Biomaterials 1999;20(18):1659–1688.

[3] Gulraj S. Matharu, Study finds 27% overall all-cause Pinnacle metal-on-metal THR failure rate at 10 years, Orthopedics Today, July 2017

[4] Dorr L.D, Long W.T. Metal-on-metal: articulations for the new millennium. Instr Course Lect 2005; 54:177-82.

[5] Dumbleton J.H, Manley M.T., Metal-on-Metal total hip replacement: what does the literature say?, J Arthroplasty 2005 Feb;20(2):174-88.

[6] K.L. Mittal, Polyimides Synthesis, Characterization, and Applications, Springer US, 2013

[7] A. Buchman, S. Sibony, G. R. Payne III, D. G. Mendes, R.G. Bryant, The Next Generation in Medical Implants, Materials World, 12 (2), 26 (2004).

[8] P. J. Burn, A. Buchman, S. Sibony, A. Oron, MP-1™ Polyimide for Medical Devices: 1. Pre Clinical Studies, American J. of Biomedical and Life Sciences, 7 (3), June 2019, P. 42.

[9] R. A. Oliver, C. Christou, T. Wang, A. Buchman, S. Sibony, W. R.Walsh, The Influence of Polyimide MP-1™ Wear Particles on a Rodent Closed Fracture Healing Model, ORS 2020 Annual Meeting, February 8 -11, 2020, Phoenix, AZ, USA, P. 54 (Awarded as best paper)

[10] Game Changing Trauma Implants Made of MP-1™, A. Buchman, S. Sibony, A. Oron, ISMBE Biomedical Engineering 2020, Haifa, Israel, 25 February 2029, P. 24.