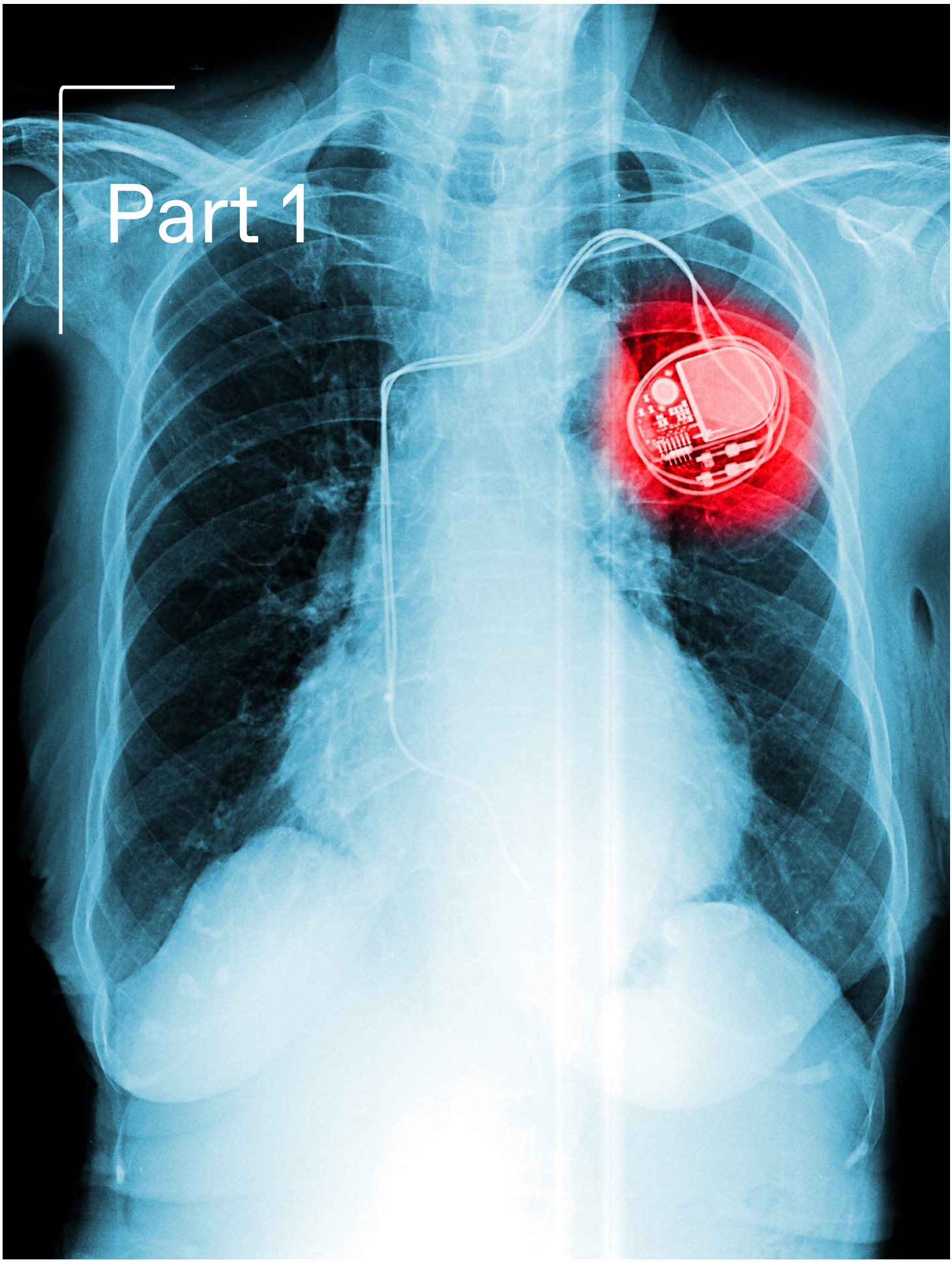
Elkem

Elkem Silicones

The evolution of implantable devices and the role of biomedical-grade silicone

Delivering your potential


Part 1

The evolution of medical implants

According to the American Medical Association, approximately one in ten Americans will have a device implanted into their bodies during their lifetime.[1] In other industrialized countries, the amount of people who have experienced an implantable medical device is believed to be between 5% and 6%. From stents and insulin pumps to cochlear implants and artificial knees, most of us know someone with an implant – so how did these lifechanging devices become so widespread?

In the 21st century, virtually every country is faced with an aging population. This is a positive signal that people are living longer thanks to improvements in medicine, hygiene, and nutrition. However, it also creates more demand for healthcare, pharmaceuticals and medical devices due to the growing incidence of disease that comes with having an older population.

Cardiovascular disease currently represents the leading cause of death globally, influenced by the aging population, ultra-processed diet and sedentary lifestyle of many developed countries. Today, cardiac resynchronization devices such as pacemakers are one of the most widely used medical implants. These products improve the blood's circulation in patients suffering from slow, fast, or irregular heart rhythms.

GlobalData market models predict the volume of new pacemaker procedures to grow at a rate of 10.74% between 2023 and 2033. Combined with replacement procedures, the company predicts the total number of pacemaker surgeries to grow from 96,861 in 2023 to 259,941 in 2033. The numbers are even higher for implantable cardioverter defibrillators (ICDs) – slightly larger devices which work in a similar way to pacemakers. New and replacement procedures for ICDs surpassed 204,000 in 2023 and are expected to hit 377,255 by 2033.

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[1] https://journalofethics.ama-assn.org/issue/implantable-material-and-device-regulation

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Early developments in implantable technologies

The widespread success of pacemakers is particularly notable considering, in 1958, they were the first electronic medical implant to ever be tested in a human. Since then, pacemakers have evolved significantly. For example, the first implantable pacemaker ran on rechargeable batteries until a version with long-lasting lithium-iodide batteries was developed. Over the next few decades, 'demand pacemakers' and 'rate-responsive pacemakers' were introduced. Demand pacemakers deliver electrical impulses only when the heart's natural rhythm slows or becomes irregular, while 'rate-responsive' pacemakers adjust the pacing rate based on the patient's activity level. The 1990s saw the introduction of dual-chamber pacemakers to deliver better synchronization of heart contractions in both the atrium and ventricle. As medical advancements continued into the next century, pacemakers became smaller, more efficient and even leadless.

> The next evolution is likely to be defined by the integration of artificial intelligence, which could be used to predict potentially dangerous rhythms before they occur.

While cardiac devices such as pacemakers and ICDs played a key role in the early history of medical implants, other notable developments included:

Joint replacements: The first successful hip replacement operation was performed in the 1960s, using polythene, steel and acrylic cement. Today, hundreds of thousands of hip replacements are conducted every year, delivering significant improvements in patient mobility, pain relief, and quality of life.

Neurostimulators: First implanted in the 1960s, spinal chord stimulators deliver electrical impulses to the spinal chord to help manage chronic pain. Deep brain stimulation devices followed not long after. Placed in the upper chest with electrodes positioned in one or more areas of the brain, the electrical current generated by deep brain stimulation devices is used to treat neurological conditions such as Parkinson's Disease, essential tremor, and dystonia.

Vascular implants: The first coronary stents were developed in the 1980s to treat coronary artery disease, helping to keep the arteries open after angioplasty. Two decades later, drug-eluting stents were introduced to reduce the risk of restenosis.

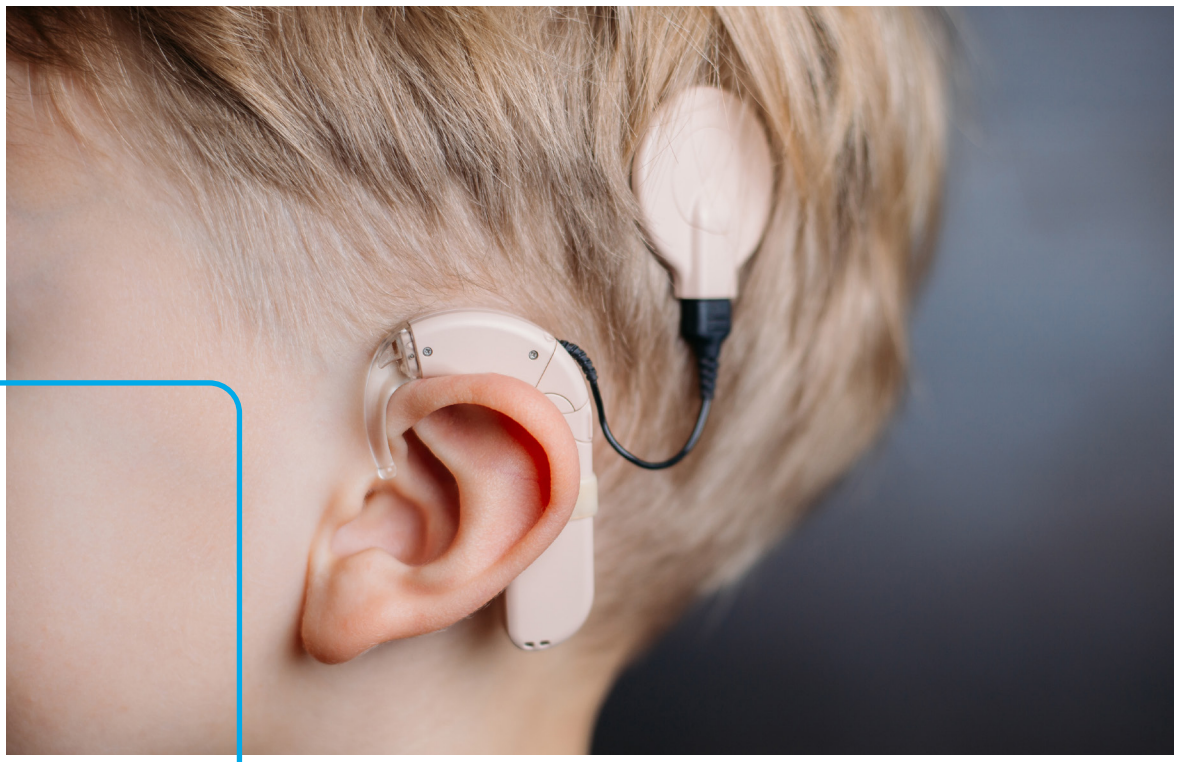
Sensory implants: First successfully implanted in the cochlear in 1957, the cochlear implant stimulates the auditory nerve with signals which are then recognized as sounds in the brain. This technology did not see widespread clinical use until significant improvements were made to it in the 1980s and 90s.

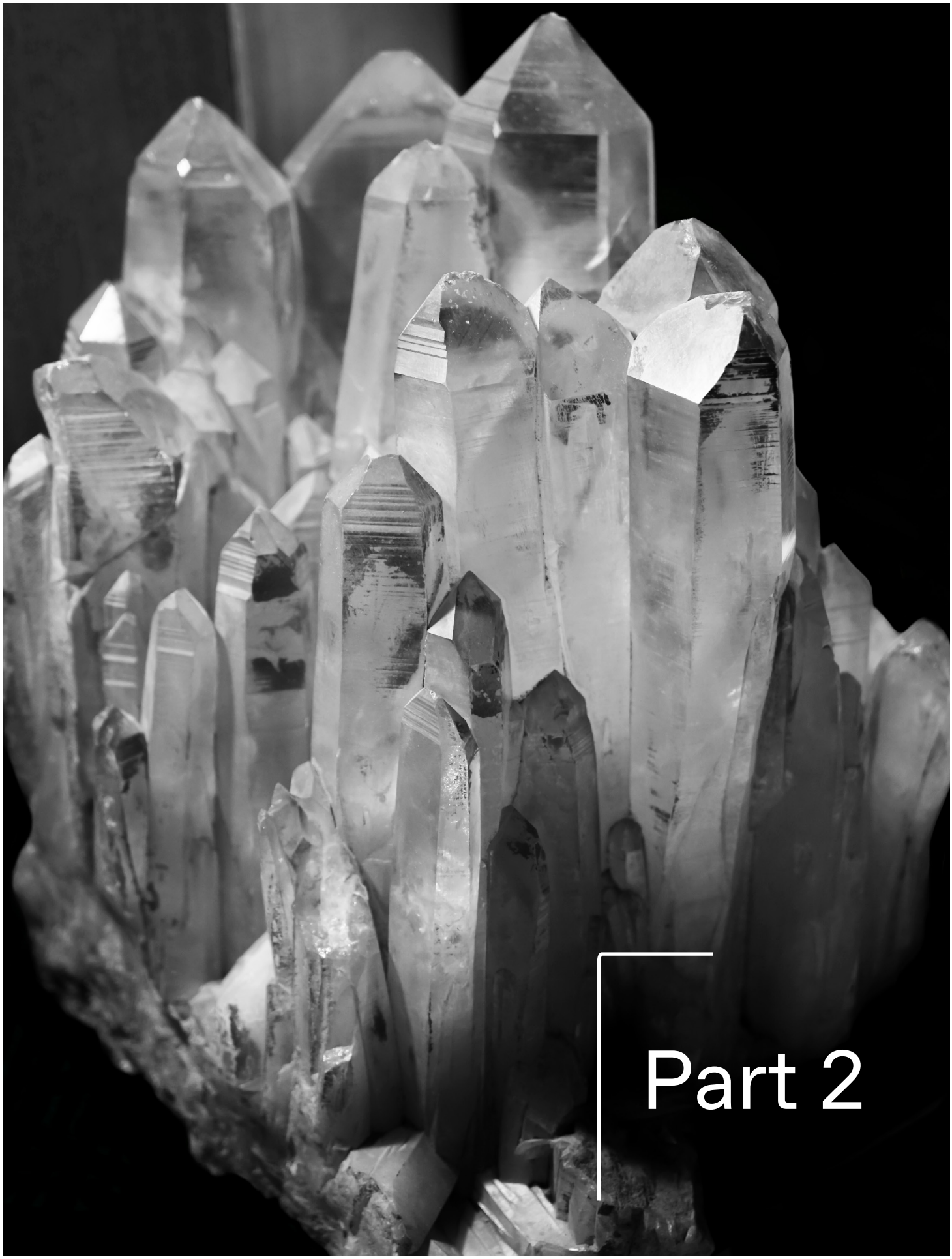
Across the history of medical devices, technological advancements have led to the commercialization of smaller, more reliable implants. Some cardiac implants are now leadless to overcome lead-related complications, while others are equipped with remote patient monitoring technology that sends information from the patient's heart directly to their doctor through WiFi or cellular data. The next evolution is likely to be defined by the integration of artificial intelligence, which could be used to predict potentially dangerous rhythms before they occur.

The availability of biocompatible materials has been critical to the evolution of medical devices. Today's medical device manufacturers have a wide range of materials to choose from, including metals such as titanium, stainless steel, and cobalt-chromium alloys. Thermoplastics like polyethylene (PTE) and polyetheretherketone (PEEK) have become mainstays, while medical-grade silicones have also played a significant role in the development of implantable medical devices, bringing a range of unique benefits to the table.

In the future, novel materials such as graphene could further expand the possibilities of medical implants. However, it is likely to be the longstanding materials backed by years of data across a diverse range of applications which will continue to be the go-to solutions for OEMs. Silicone, which has demonstrated its versatility over the decades, will therefore play a key role in the future of medical devices.

In the second part of this whitepaper, we dive into the value chain for biomedical-grade silicone and discuss its compelling advantages and wide-ranging applications in implantable devices.





Part 2

From quartz to silicon to biomedical-grade silicone

Silicone is a synthetic polymer made up of polyorganosiloxanes, where silicon atoms are joined to oxygen to form chemically stable <<siloxane>> bonds. These bonds make up the backbone of silicone, with the remaining valences link with organic groups such as phenyl, vinyl, and hydrogen.

While silicon was first discovered by a Swedish chemist in 1824, silicone materials did not become available until the 1940s, when it was used to insulate electrical components on World War II aircraft. In this application, silicone proved its ability to protect ignition wire harnesses from arcing at high altitudes. Not long after, silicone's biocompatibility was put to the test in implanted devices. One of the first instances of this was performed by Dr F Lahey in 1946, who used the material during bile duct reconstruction surgery. Two years later, the first human male urethra replacement was completed using a silicone elastomer tube, and in 1968 silicone was used as a replacement for cartilage and soft tissue in finger joints. Numerous other applications soon followed and, by the 1960s, silicone was widely regarded as a critical material in the medical device supply chain.

How is silicone made?

Since silicone is a synthetic material, it is not present in the environment in any form. However, in silicon's natural form as the raw material quartz, it is one of the most abundant minerals on Earth. From quartz, metallurgical-grade silicon is produced by carbothermal reduction. This requires the mixing of quartz with carbon under extreme temperatures, causing the carbon to react with the silicon dioxide in the quartz. The metallurgical-grade silicon is then reacted with methyl chloride to produce methylchlorosilanes. Impurities are removed through a cleaning process and the various methylchlorosilanes created are separated through fractional distillation.

A polymerization process is then carried out on the resulting suite of purified methylchlorosilanes, leading to a suite of high-performance polymer structures. The most basic of these is polydimethylsiloxane, or PDMS, a transparent fluid which is chemically inert, hydrophobic, and thermally stable. From there, various adjustments can be made to PDMS by altering the chain length, swapping the methyl groups with other functional groups, or introducing additives in order to optimize properties and functional performance.

> Silicone is inherently biocompatible due to its chemical inertness, meaning it does not react with or dissolve in bodily fluids.

Benefits in implantable devices

With patient safety the main priority of medical device design, biocompatibility will always be the most important criterion in a material's suitability for medical devices. Silicone is inherently biocompatible due to its chemical inertness, meaning it does not react with or dissolve in bodily fluids. This property makes silicone suitable for long-term implantable devices and products, including breast implants. However, in 1992, the safety of silicone was questioned when the US Food and Drug Administration (FDA) withdrew all silicone gel-filled breast implants from the market. Concerns had rose over the potential for these products to leak and rupture, potentially causing injury or illness.

Following a 14-year ban and extensive scientific review, silicone breast implants were reintroduced to the market in 2006, supported by evidence demonstrating the material's safety. In fact, one 14-year study that followed 3,182 women with silicone breast implants actually showed fewer cases of cancer than would be expected in a group of that size. While the explanation for the lower-than-expected number of cancers observed in this study was unclear, the 13-member committee established by the Institute of Medicine concluded its review of thousands of scientific reports by stating "that the silicones found in breast implants do not provide a basis for concern".[2]

In 2011, with silicone gel-filled breast implants now back on the market, the FDA issued its *Update on the Safety of Silicone Gel-Filled Breast Implants*, which included data from multiple post-approval studies as well as a summary and analysis of adverse events and a literature review. The two largest post-approval studies enrolled more than 40,000 women each, with the data showing no evidence that silicone gel-filled breast implants cause connective tissue disease, reproductive problems, or breast cancer – all key concerns during the lead up to the ban in the 1990s.[3]

[2] Institute of Medicine (US); Grigg M, Bondurant S, Ernster VL, et al., editors. Information for Women About the Safety of Silicone Breast Implants. Washington (DC): National Academies Press (US); 2000. A Report of a Study by the Institute of Medicine. Available from: https://www.ncbi.nlm.nih.gov/books/NBK44775/

[3] FDA. Update on the Safety of Silicone Gel-Filled Breast Implants (2011).

"After the breast implant lawsuits in the 1990s, silicone is probably the most studied material that is used in implantables today," remarks Michael Goglia, North America healthcare market manager, Elkem Silicones. "It has been highly scrutinized and then found that it wasn't a contributing factor to the medical issues that occurred. The main reason for that is its biocompatibility."

In addition to safety, there are a range of other benefits to using silicone in medical implants:

Hydrophobic: Silicone naturally repels water and all bodily fluids, contributing to its biocompatibility. This water repellency also ensures bacterial resistance.
Example: urology catheter.

Sterilizable: Because the <<siloxane>> bond maintains its integrity across a range of temperature extremes, it is possible to sterilize silicone devices by multiple different mediums, including gamma, autoclave, and ethylene oxide.
Example: gastric band.

Flexible: The flexibility and malleability of a silicone elastomer can aid its insertion during minimally invasive surgeries, with implants made from this material possibly fitting through small incisions and later expanding in the body. In certain applications, silicone's flexibility and softness can also offers improvements to patient comfort.
Example: tissue expander.

Insulating: Silicone is used widely as an electrical insulator, raising the performance of electrical systems such as cardiac implants and neurostimulation devices and improving their safety.
Example: cochlear implant.

Conductive: With the addition of fillers, silicone can also be deployed as a conductor. This facilitates wireless communication in remote patient monitoring or neurostimulation devices that are controlled via the patient's smartphone.
Example: deep brain stimulation for chronic pain.

Corrosion inhibitor: Silicone can act as a corrosion inhibitor when used to encapsulate metal components, improving the durability and biocompatibility of an array of materials.
Example: encapsulating electronics in implanted pulse generators.

Miniaturization: Silicone is playing a key role in the miniaturization of medical devices thanks to its ability to be micro molded at very high resolutions, maintaining precision despite the smaller profiles. *Example: finger joints.*

Good excipient: Since silicones form a permeable matrix structure when cured, they are a great option for drug-eluting devices that consistently deliver an API over time.
Example: female contraceptive devices.

3D printing: As the benefits of 3D printing in the medical field continue to emerge, silicone's compatibility with additive manufacturing represents a key advantage.
Example: patient-specific cosmetic implants.

Elkem has more than 65 years of silicone formulation expertise, with many years serving the medical device industry with its Silbione™ products.

Ensuring a high-quality product for the medical environment

While silicone is naturally biocompatible, medical device manufacturers need to be certain that no contaminants can be introduced into the silicone materials they choose through production and packaging. It is highly recommended to choose a medical-grade material that has passed criteria set forth in ISO 10993 and that has been produced and packaged in a certified Class 7 cleanroom within an ISO 13485-compliant facility.

ISO 13485 is the quality management system (QMS) standard required for organizations involved in the design, production, installation and servicing of medical devices. Amongst many points, ISO 13485 emphasizes the importance of a robust traceability system throughout manufacturing, starting from the characterization of each raw material prior to production. Quality management is particularly vital when it comes to implantable devices, which the FDA splits into short-term (less than 29 days) and long-term (greater than 29 days).

“Before production, we actually take an FTIR scan of each raw material to ensure it is what it’s supposed to be, and there’s additional testing that’s done outside of that,” says Goglia. “Typically, a standard medical-grade silicone has cytotoxicity tests done annually to confirm nothing has changed. For a long-term implantable silicone, there’s cytotoxicity testing done on every single batch that’s produced, and the batch isn’t released until those results come back meeting the stringent quality release criteria.”

For Elkem’s Silbione™ Biomedical products – a brand of materials suitable for more than 29 days of exposure – additional testing has been carried out according to the ISO 10993/USP Class VI standards for 12-week implants. As well as the acute systemic toxicity and cytotoxicity tests, these include tests for hemolysis, intracutaneous reactivity, mutagenicity, pyrogenicity, skin sensitization, and tissue irritation. Silbione™ Biomedical products also come with the submission of Master Access Files (MAF) or Drug Master Files (DMF) to support the customer’s regulatory submissions to the FDA. In addition, certain products in the Silbione™ Biomedical line have undergone further purification to control D4, D5 and D6 levels – a precaution which may be required depending on the application and processing.

Elkem has more than 65 years of silicone formulation expertise, with many years serving the medical device industry with its Silbione™ products. These products are available in a range of forms, from liquid silicone rubbers (LSRs) and high consistency rubbers (HCRs) to dispersions, fluids, adhesives and gels. Headquartered in Norway but with a worldwide industrial footprint, the company is one of the leading suppliers of silicone in the world and the only fully integrated supplier of medical and biomedical-grade silicone.

“Elkem is the only implantable-grade silicone producer that controls its raw materials back to quartz,” says Goglia. “We mine our own quartz, convert that into silicon, and convert silicon into methylchlorosilanes, which are then produced into the raw materials that we use to create our implantable-grade products.

“The real importance of that for our customers is change control and security of supply,” he adds. “Because we own our raw materials, we can ensure our biocompatible material production is not impacted and the supply chain is robust. If there is a material shortage, which has occurred over the years, we can always prioritize our healthcare-grade materials. With four different ISO 13485-certified sites around the world, we also have a diversified footprint in manufacturing, meaning we could produce our biomedical-grade silicones in many different subsidiaries.”

Security of supply is of critical importance to medical device manufacturers for several reasons, including regulatory compliance, business continuity, and reputation management. Most of all, it means healthcare providers can rely on the consistent availability of the critical, life-sustaining devices they need to support patient safety and care continuity.

To discuss how we could support your implantable device project, please reach out here.