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GlobalData
MediPoint

BONE GRAFTS AND SUBSTITUTES - GLOBAL ANALYSIS AND MARKET FORECASTS

Executive Summary

Bone Grafts and Substitutes: Key Metrics in 10 Major Markets	
Bone Grafting Procedure Volume in 2013	
Spinal Fusion	1,047 million
Trauma Fixation	414 million
Joint Reconstruction	352 million
Craniomaxillofacial (CMF) Procedure	48 million
Total	**1,861 million**
2013 Market Sales ($m)	
US	$1,391.9m
5EU	$406.1m
Japan, Brazil, China and India	$291.5m
Total	**$2,089.5m**
Key Events (2013–2020)	**Impact**
(2013) Alphatec Spine voluntarily stopped shipping PureGen Osteoprogenitor Cell Allograft	↑↑↑
(2013) Wright Medical's premarket approval (PMA) application for Augment Bone Graft was not approved by the US Food and Drug Administration (FDA)	↑↑↑
(2014) FDA's 510(k) clearance for NuVasive's AttraX	↑↑
(2014) Osiris Therapeutics' transition of its Ovation product line to the OvationOS formulation	↑
(2014–2015) RTI Surgical's commercial launch of map3 Cellular Allogeneic Bone Graft	↑↑
(2015–2016) Expected FDA's PMA approval for CeraPedics' i-FACTOR	↑↑
(2015–2016) Expected FDA's approval for Advanced Biologics' OsteoMEM	↑↑
(2015–2016) Expected FDA's PMA approval for BioSET's AMPLEX	↑↑
2020 Market Sales ($m)	
US	$1,776.8m
5EU	$467.0m
Japan, Brazil, China and India	$464.9m
Total	**$2,708.7m**

Source: GlobalData, based on secondary research and primary research, including interviews with key opinion leaders (KOLs) and industry experts in 10 markets (US, France, Germany, Italy, Spain, UK, Japan, Brazil, China and India).

Note: 5EU = France, Germany, Italy, Spain, and the UK.

The field of bone grafts and substitutes (BGS) is among the most promising markets in the orthopedic industry. In 2013, revenue from the global BGS market, consisting of traditional allograft bone, machined allograft bone, growth factors/bone morphogenetic proteins (BMPs), demineralized bone matrices (DBMs), synthetic bone substitutes, and cell-based matrices, is estimated to be $2,089.5m across the 10 major markets covered in this report, including the United States, France, Germany, Italy, Spain, the United Kingdom, Japan, Brazil, China and India. Despite the FDA's ongoing scrutiny of the growth factor/BMP and cell-based matrices segments, the BGS market sales are expected to rise steadily throughout the forecast period, reaching $2,708.7m with a compound annual growth rate (CAGR) of 3.8%.

Key drivers during the forecast period:

- The growing procedure volume of spinal fusion and joint reconstruction due to pandemic aging and obesity
- Companies' continued efforts on product innovations and line extensions to create a comprehensive orthobiologics platform
- Orthopedic community's ongoing search for materials promoting osteoinductivity and osteogenesis
- Improved accessibility to the latest-generation BGS products in emerging economies

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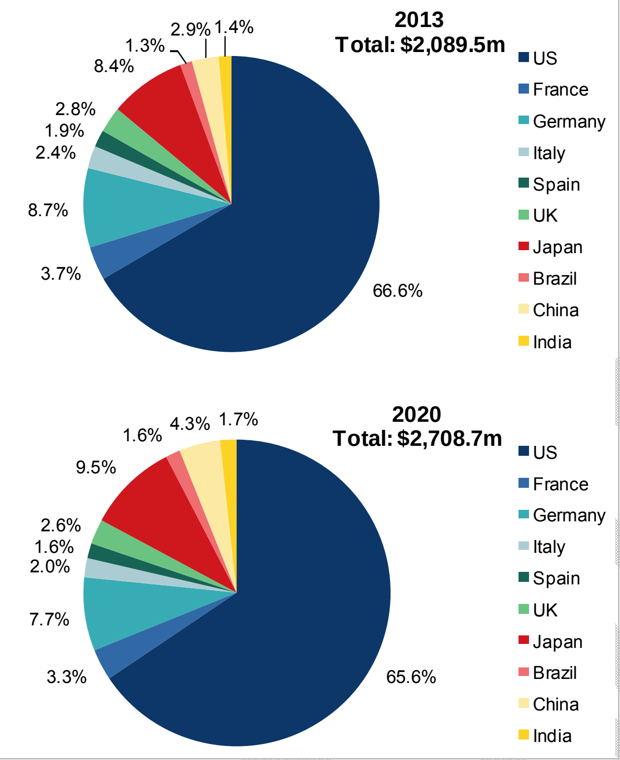
- Increased public awareness of bone regeneration achieved through biologics

BGS Market by Major Market, 2013 and 2020



Source: GlobalData.

As of 2013, the US comprised a majority of the market share, with 66.6%, and is expected to continue to contribute a substantial amount to the global BGS market over the forecast period. The 5EU countries all together contributed 19.4% to the market revenue, with Germany leading the pack at 8.7%. Another major market with significant presence is Japan, at 8.4%.

GlobalData estimates that global market share will remain relatively stable for the forecast period across the 10 major markets. While all of the major markets are expected to expand from a procedure standpoint, western countries will be experiencing stronger pricing pressures stemming from the governments' healthcare budget constraints for high-volume orthopedic surgeries, limiting the growth potential of the BGS market in the EU.

Continued Product Innovation Drives Market Growth

Bone grafting procedures are undergoing a gradual shift from autologous and allogeneic bone grafts to synthetic bone graft substitutes. The emergence of new biological or synthetic materials to facilitate regeneration of damaged or diseased bone can increasingly minimize the usage of autograft in the surgeries. In particular, the motivation to incorporate the favorable properties of different materials into an effective bone graft product has led to the manipulation and development of various new composite grafts. One of the recent attempts from orthopedic companies to enhance bone substitutes' osteoconductivity is the incorporation of bioactive materials, such as bioactive glass.

Meanwhile, with the increase in corporate and federal funding in regenerative medicine, stem cell therapies represent a fast-growing, high-margin opportunity. Today, some of the leading orthopedic companies have allocated a large portion of their R&D budget to these stem cell-based products.

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A good example is the cell-based matrices recently introduced to the US market. The incorporation of adult mesenchymal stem cells into allograft bone gives rise to a matrix harnessing the healing triad – osteoconductivity, osteoinductivity, and osteogenesis.

While evolution in bone graft materials is driven by the manufacturers, which create different bone substitutes products to enhance their product mix, it is mandatory that these advances be adequately studied in clinical practice. In a market that is inundated with biologics with very limited basic science data supporting the efficacy, availability of human clinical data to demonstrate product efficacy remains the key to success.

Key Players in the Global BGS Market

Overall, the competitive landscape in BGS mirrors that in the spine market, as more than 60% of the BGS products are used in spinal procedures. At present, there is one clear leader in the market: Medtronic. As Medtronic is the pioneer in spine technologies and is the only supplier of BMP-2 product (INFUSE Bone Graft), the company has sustained the leading position in the global BGS space, especially in the BMP and DBM segments. While Medtronic is very likely to dominate the market in the next several years, its share will be shrinking, as the growth potential of INFUSE has been affected by some negative media attention regarding off-label usage and adverse events with specific indications.

Moreover, the lower adoption rate of DBM products in markets outside the US due to variations in regulation has hindered Medtronic's business expansion in the global DBM segment.

Following Medtronic is Stryker and DePuy Synthes. Compared with Medtronic, these two companies thrive in the synthetic bone substitutes segment. Beyond these three major players, the BGS market comprises a great number of players, each specializing in a couple of segments. Moving forward, the erosion of the share of the major players by smaller start-ups observed in the spine market is also expected to occur in the global BGS market. With cell-based matrices on the rise, it will be interesting to see how these products would help orthopedic companies to hone the technological edges and redefine the competitive landscape in the global BGS arena.

The Global BGS Market Future Outlook

The economic downturn has been a continued concern with pricing wars in other sectors of orthopedics. While BGS is a market that can be susceptible to this, it has affected this market only partially, as the whole orthopedic community is now placing appreciable emphasis on the importance of biologics.

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Because bundling complementary biologics to hardware allows for continuous income generation, and ensures that the company's biologics platform is a fixture in a hospital's orthopedic implant inventory, cross-selling has helped a number of orthopedic and spine companies to bolster their positions in the BGS space. Additionally, a crop of start-ups that are biologics pure play companies are also hoping to achieve a statistically significant difference in their products' performance compared with those of established firms.

Moving forward, the increased marketing that will follow approval of new BGS products will contribute to even greater awareness of all of the viable alternatives to the conventional autograft harvesting technique. In the years to come, launching and marketing a comprehensive BGS portfolio with a clear value proposition will remain critical to companies' success as they jockey for market leadership. Meanwhile, companies will need to understand two basic driving forces – surgeons who continuously seek improved patient outcomes and healthcare systems who become increasingly concerned about the economics.

What Do Physicians Think?

Following the negative media surrounding Medtronic's INFUSE Bone Graft, surgeons now hold varied opinions regarding the BMP products. While there are a group of firm believers in the clinical efficacy of BMP-2, an increasing number of surgeons have raised doubts about the cost-effectiveness that BMP products can bring to the patients and hospitals.

"The real difference in fusion rate comes from the use of BMP-2. The fusion rate of BMP-2 is so good that the cost for revision goes down."

Key Opinion Leader

"It's not all about the price tag; you have to look at the value they [BMPs] can add to the patients. Because of better osteoinduction and fusion rate, the patient can be discharged one day earlier, and that's where actual cost saving comes in."

Key Opinion Leader

"I haven't seen a drastic decrease [in the usage of BMPs] so far. But the debates put a bit of barrier on growth. The other element is cost-containment measures that most EU countries put in place."

Industry Key Opinion Leader

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As health executives are scrutinizing purchases and using multiple channels to procure biologics at highly competitive prices, surgeon's preference is no longer considered the top priority in many hospitals' decision-making processes.

"Because of the large availability of different preparations, and inconsistencies within preparations, it's hard to make any kind of decision just based on product information [of these BGS products]. So the biggest driving force is the cost, and surgeon preference is not a top priority."

Key Opinion Leader

Human clinical efficacy is an important consideration for physicians in choosing to adopt a new biologic. Currently, in the BGS market, the lack of reliable studies to demonstrate products' efficacy in human clinical settings has led to many surgeons reluctant to adopt newly launched biological products.

"The push for new orthobiologics is in large part industry-driven, rather than based on objective patient clinical data."

Key Opinion Leader

"There are an enormous number of biological products currently on the market, but the number of unbiased scientific data in human studies is pathetically small. This is a real problem in orthobiologics today."

Key Opinion Leader

Regarding the recently introduced cell-based matrices in the US market, physicians explained the potential barriers to further expanded adoption of these products.

"The use of cell-based matrices is rare, because they are very expensive. There has to be a good reason to use cell-based matrices. If there is a biologic issue in the patient, like lack of healing or not enough bone healing, I may try a cell-based therapy. But that's only because I can't or I won't do something to increase the healing."

Key Opinion Leader

"I think there is definitely a market for cell-based matrix in the future. We haven't used any of those products yet. We are currently sitting on the sidelines and waiting for their clinical efficacy to be proven, but we have great interest in that."

Key Opinion Leader

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2 Introduction

Autograft bone is considered the gold standard in orthopedic surgeries, as it confers complete histocompatibility while possessing osteoinductive, osteoconductive and osteogenic healing potentials. Allografts and bone substitutes may be used when autograft is insufficient or when immediate structural support is needed. At times, the quantity of bone graft required exceeds the amount of the patient's own bone, possibly because of factors such as patient size, age, previous graft harvesting, or donor-site pathologic processes. In addition, the patient may opt against graft harvesting from a distant site (e.g., iliac crest) because of the comorbidities involved. All these factors have led to a soaring demand for alternatives to autograft bone in the global orthopedic community.

The ideal bone graft substitutes are biocompatible, bioresorbable, osteoconductive, osteoinductive, structurally similar to bone, easy to use, and cost-effective. Within these parameters, a growing number of bone alternatives are commercially available for orthopedic applications, including spinal fusion, joint reconstruction, trauma fixation, and CMF procedures. An extensive list of bone grafts and substitutes are currently available, along with a classification scheme that divides these products into six major groups depending on the primary material composition and processing method – traditional allograft bone, machined allograft bone, BMPs, DBMs, synthetic bone substitutes, and cell-based matrices. Excluded from this report are platelet concentrators, allograft tissue, tissue substitutes, hyaluronic acid viscosupplementation, surgical hemostats, cartilage repair products, and cell concentration systems.

The market for BGS is characterized by rapid technological change, frequent new introductions, changes in customers' demands and evolving industry standards. An example is the industry's recent re-evaluation of the expanding utilization of BMPs. After its approval by the US FDA in July 2002, BMP-2 has been adopted by many spine surgeons as a replacement for the more traditional iliac crest bone graft to avoid the complications associated with autograft bone harvest. However, as broad clinical use escalated, reports increased of potentially serious complications associated with BMP-2. Controversy continues, particularly regarding the safety of BMPs and whether it should routinely replace iliac crest bone graft in off-label indications.

Introduction

Following the publication of the Yale University Open Data (YODA) project's findings on Medtronic's INFUSE Bone Graft in mid-2013, the issue of clinical trial transparency has been brought to center stage in the orthobiologics space. Players in this field will need to continue to invest in providing solid clinical data to secure a long-term foothold in the BGS market.

2.1 Catalyst

Across the countries covered in this report, bone grafting procedure volume has experienced notable growth in recent years, although increases in sales volume and market revenue have not been consistent for all types of BGS. Although autograft is still perceived as the gold-standard material in bone grafting, the wide array of alternatives available in the market has resulted in a gradual shift towards increased adoption of bone graft substitutes, especially in the US and European markets. In contrast to the general picture in developed countries, autograft bone still represents the most popular option during bone grafting in the Asia-Pacific (APAC) region and South America. Moving forward, in the highly competitive orthobiologics industry, there will be a growing preference towards the use of bone substitutes. In particular, the shift to lower-dosed BMPs is expected to be accompanied with continued rise in the sales volume of synthetic bone substitutes in all markets, and increased adoption of cell-based matrices in the US market. Since BGS companies have uncovered new ways of using their technologies to find synergies with spine hardware products, and orthopedic implants to deliver better therapeutic outcomes, future access in the market will hinge on suppliers positioning their products as part of a broader therapy system for bone repair that includes multiple offerings. Additionally, ample opportunities lie within the emerging markets, which are the countries that have a higher compound annual growth rate (CAGR) in the BGS market and will provide the key for growth and gaining market share.

2.2 Related Reports

- GlobalData (2013). MediPoint: Knee Replacement – Global Analysis and Market Forecasts, November 2013, GDME0181MAR
- GlobalData (2013). MediPoint: Trauma Fixation – Global Analysis and Market Forecasts, October 2013, GDME0185MAR
- GlobalData (2013). MediPoint: Total Hip Replacement – Global Analysis and Market Forecasts, July 2013, GDME0174MAR

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- GlobalData (2013). MediPoint: Total Shoulder Replacement – Global Analysis and Market Forecasts, June 2013, GDME0177MAR
- GlobalData (2013). MediPoint: Total Wrist Reconstruction – Global Analysis and Market Forecasts, March 2013, GDME0171MAR
- GlobalData (2013). MediPoint: Total Ankle Replacement – Global Analysis and Market Forecasts, February 2013, GDME0167MAR
- GlobalData (2013). MediPoint: Cervical Total Disc Replacement – Global Analysis and Market Forecasts, January 2013, GDME0169MAR

Appendix

11.6 About MediPoint

MediPoint is the flagship product for GlobalData's Medical team. Each MediPoint report is built from the ground-up by our team of healthcare analysts in the US and UK. Each report includes input from experienced physicians and leading Key Opinion Leaders (KOL). Running throughout each report in the series, "What Do Physicians Think" quotes provide a unique insight into how healthcare professionals are reacting to events within the industry, and what their responses could mean for industry strategists.

11.7 About GlobalData

GlobalData is a leading global provider of business intelligence in the Healthcare industry. GlobalData provides its clients with up-to-date information and analysis on the latest developments in drug research, disease analysis, and clinical research and development. Our integrated business intelligence solutions include a range of interactive online databases, analytical tools, reports and forecasts. Our analysis is supported by a 24/7 client support and analyst team. GlobalData has offices in New York, Boston, London, India and Singapore.

11.8 Disclaimer