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INFORMATION FOR GROWTH

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2015, October 5th
Reims, France

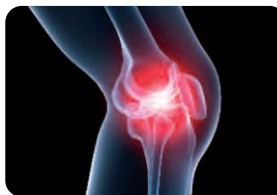
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Additive and Trabecular Manufacturing for Volume Production in the Orthopaedics Industry

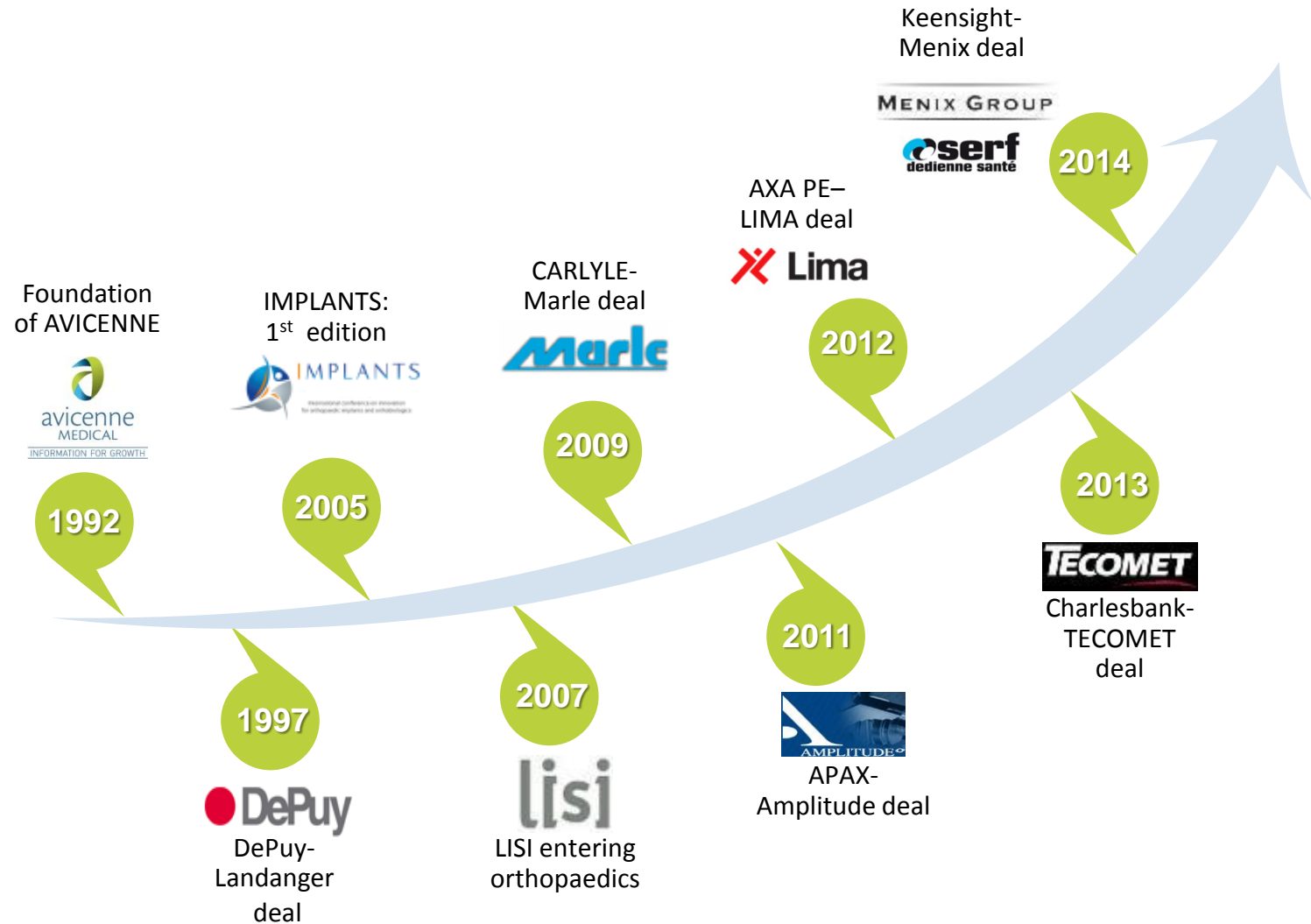
Ali MADANI
Director



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Our history

AVICENNE has always been involved in the major deals & events in the Orthopaedics Industry



Additive and Trabecular Manufacturing for Volume Production in the Orthopaedics Industry

EPMA, 4-7 October 2015
Reims - France

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Implants conference



The international meeting on innovations & solutions for orthopaedic implants & orthobiologics June 16th, 2015 Paris - 11th edition

- 🕒 Founded and chaired by AVICENNE since **2005**
- 🕒 **Implants 2016** next edition: Paris - Tuesday, June 7th 2016
<http://www.implants-event.com/home-2/>



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AVICENNE market reports

“Worldwide orthopaedic Contract Manufacturing market report 2014-2018 & Top 100 supplier profiles” October 2015 2nd edition

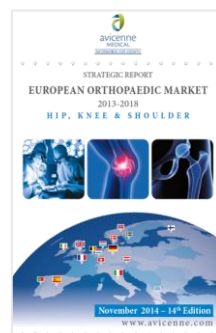
- 🔗 OEMs strategy for outsourcing & home-made
- 🔗 Detailed markets & sizing for :
 - 🔗 Forging: hip stem, hip cup, femoral knee...
 - 🔗 Casting: femoral knee, tibial knee, hip cup...
 - 🔗 Hip, knee, spine & trauma and instruments machining & finishing,
 - 🔗 Cases & trays: hip, knee, spine, trauma
 - 🔗 Coating: stem, cup, femoral, tibial
 - 🔗 Ceramics: hip heads, hip liner
 - 🔗 Cleaning & packaging...
- 🔗 Top 100 Contract manufacturer profiles



Available immediately

“European Orthopaedics Market 2013-2018” November 2014 14th edition

- 🔗 First publication in 1993
- 🔗 Yearly up-date
- 🔗 Hip, knee, shoulder
- 🔗 Based on 80+ interviews
- 🔗 810 pages & 1550+ graphs & exhibits detail the European Market in Germany, France, Italy, Spain, UK, and other countries



Available immediately

“Trends, Developments & Dynamics of the European Spine Market” September 2011 6th edition

- 🔗 First publication in 2000,
- 🔗 Yearly up-date,
- 🔗 Universal Fusion Systems, cages, Disc prosthesis...
- 🔗 70+ interviews of spine companies, distributors & surgeons,
- 🔗 400 pages & 300+ graphs detailing the European market in Germany, France, Italy, Spain, UK, Belgium, Switzerland and in other countries.



Available immediately

“Orthopaedics patent watch” Yearly edition

- 🔗 Focus on 4 segments: hip, knee, trauma and orthobiologics,
- 🔗 Report published each 2 months,
- 🔗 More than 50 patents presented by number registration and with scheme & diagrams,
- 🔗 One shot:
 - 🔗 To identify the new products & R&D trends,
 - 🔗 To follow your competitor's strategic development choices.



Available immediately

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Apax Partners, AXA PE now Ardian, Argos Soditic, Banque Lazard, Carlyle Group, Charlesbank Capital, European Capital, Goldman Sachs, Keensight Capital, LBO France, Permira, Pragma Capital, Rothschild Five Arrows, Simuval, Warburg Pincus...

ATS Stellite, Ceramtec, Cetim, EOS, Finetubes, Forginal, Geoffroy, Greatbatch, HWG, Invibio, Ionbond, Jabil Medical, Jenoptik, Heptal, Komet, LISI Medical, Manoir Industries, Marle, Nowak, One Ortho, Projection Plasma System, Sandvik, Stainless, Somepic, Symmetry Medical, Tecomet, Terolab Surface Medical, Vaccucast, VSMPO Tirus, Wichard, Willemin Macodel...

Arthur D. Little, AT Kearney, Bain, Informa, LEK Consulting, McKinsey & Company, OC&C Strategy, Oliver Wyman...



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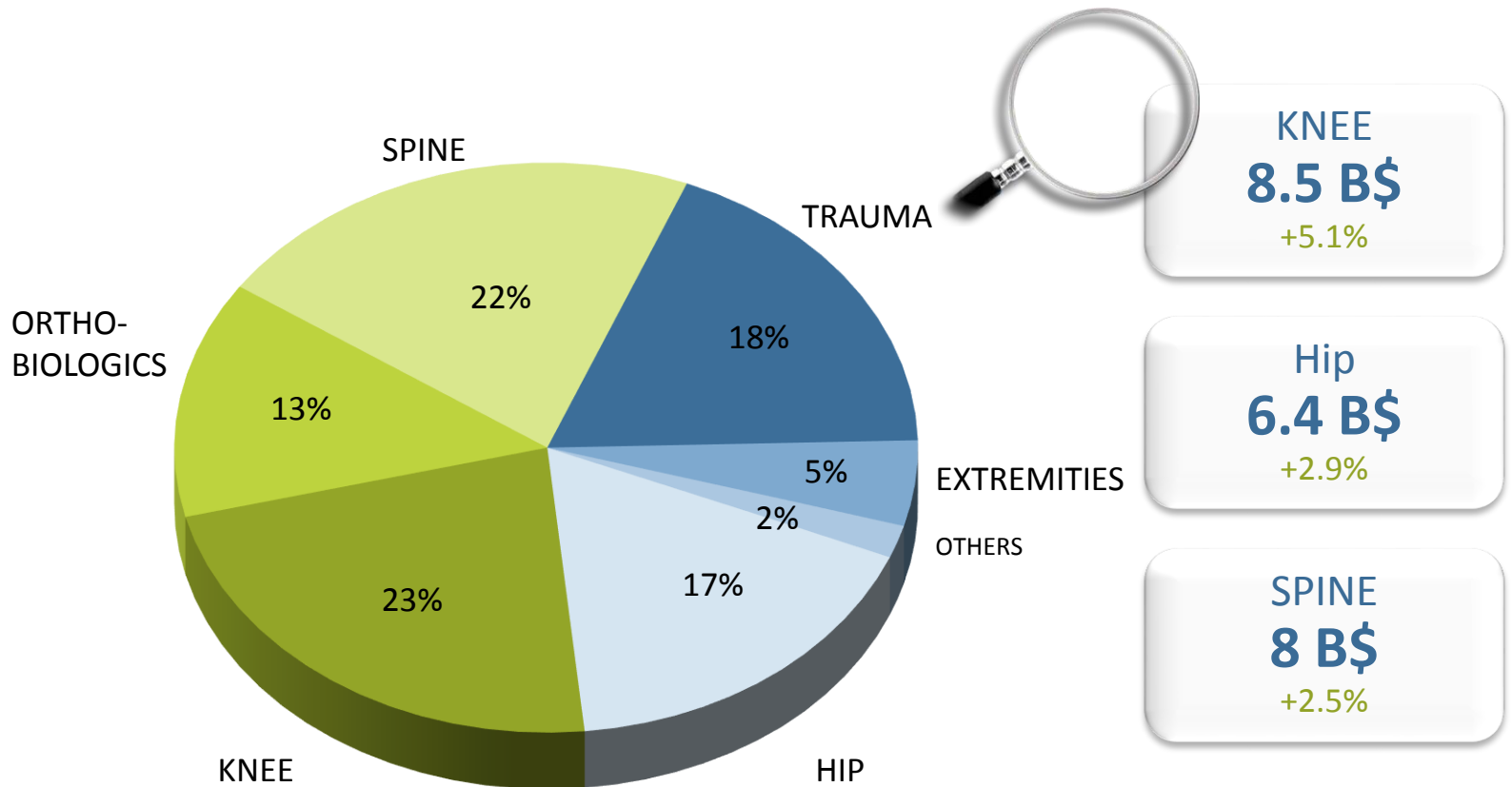
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Agenda

- I. Manufacturing of implants & instruments: current picture and forecasts**
- II. Past and current position of Zimmer the precursor with Trabecular Tantalum**
- III. Examples of Additive Manufacturing for orthopaedics: 3 main applications**
 - 🕒 Instruments & implants prototypes (metal or plastic)
 - 🕒 Patient specific guides / instruments (ex: cutting tools for knee)
 - 🕒 Manufacturing of porous implants: the way to the mass market
- IV. The most advanced orthopaedic companies on Additive Manufacturing: market focus, technology used, number of machines and investments**
- V. Which challenges and opportunities exist for Additive Manufacturing as a production technology for medical devices?**
- VI. Take home messages:**
 - 🕒 Will additive manufacturing be a key technology for the orthopedics industry in the years to come?
 - 🕒 What strategies are the major orthopedic companies adopting relative to additive manufacturing?
 - 🕒 Buy or Build? Will the EOMs develop the capabilities internally to maintain a strategic advantage or do they prefer buying or subcontracting this technology?

Worldwide orthopaedic markets in 2014: ~37 BUS\$ (+4.4%)



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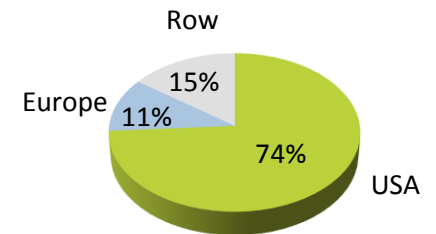
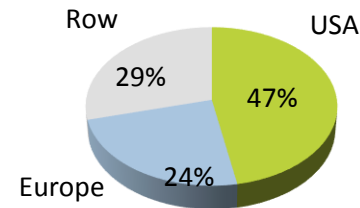
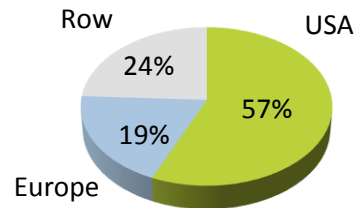
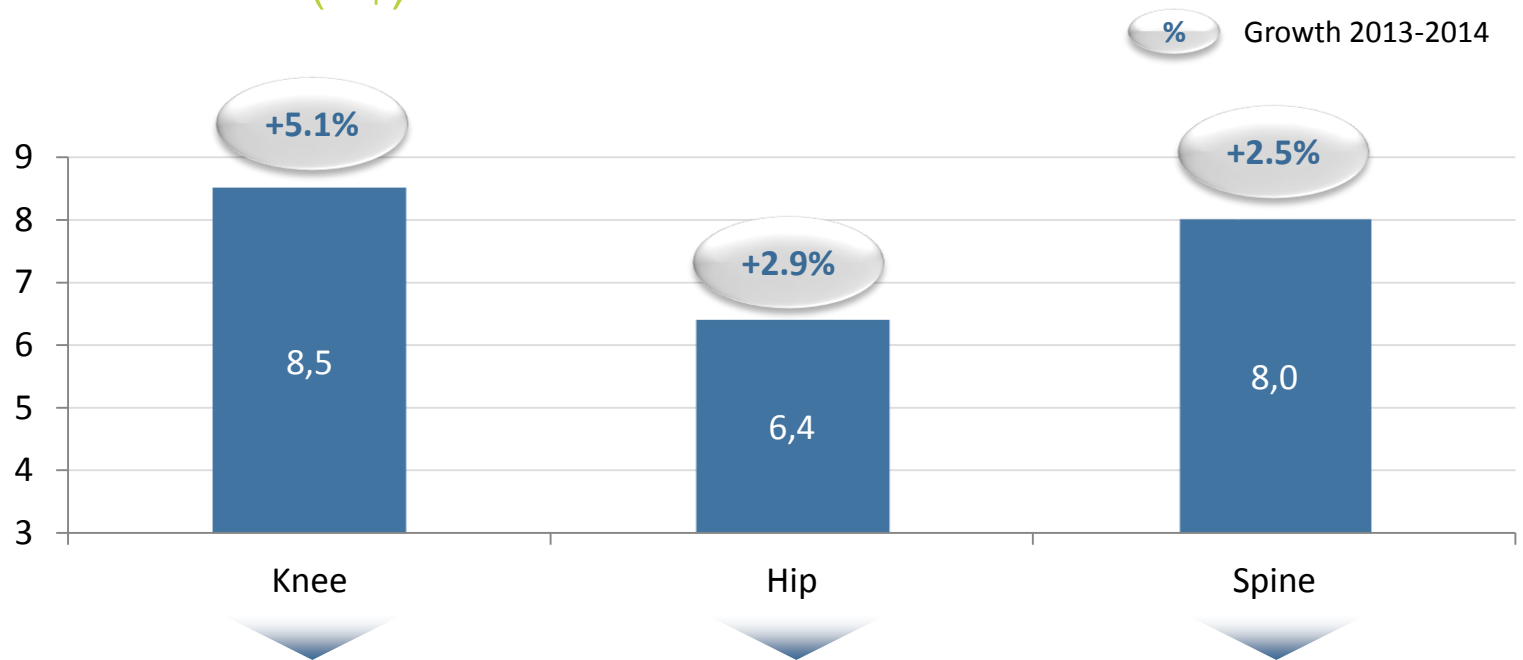
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- Extremities: Shoulder, Elbow, Ankle, Foot, hand,... (excluding trauma)
- Orthobiologics: Allograft, Xenograft, Synthetic Bone, Cement, BMP, others, Cell based Product, Auto repair product, Anti Adhesion product, Hyaluronic Acid,...

Source: Avicenne research & analysis 2015

Worldwide implants market in 2014 in value (B\$)

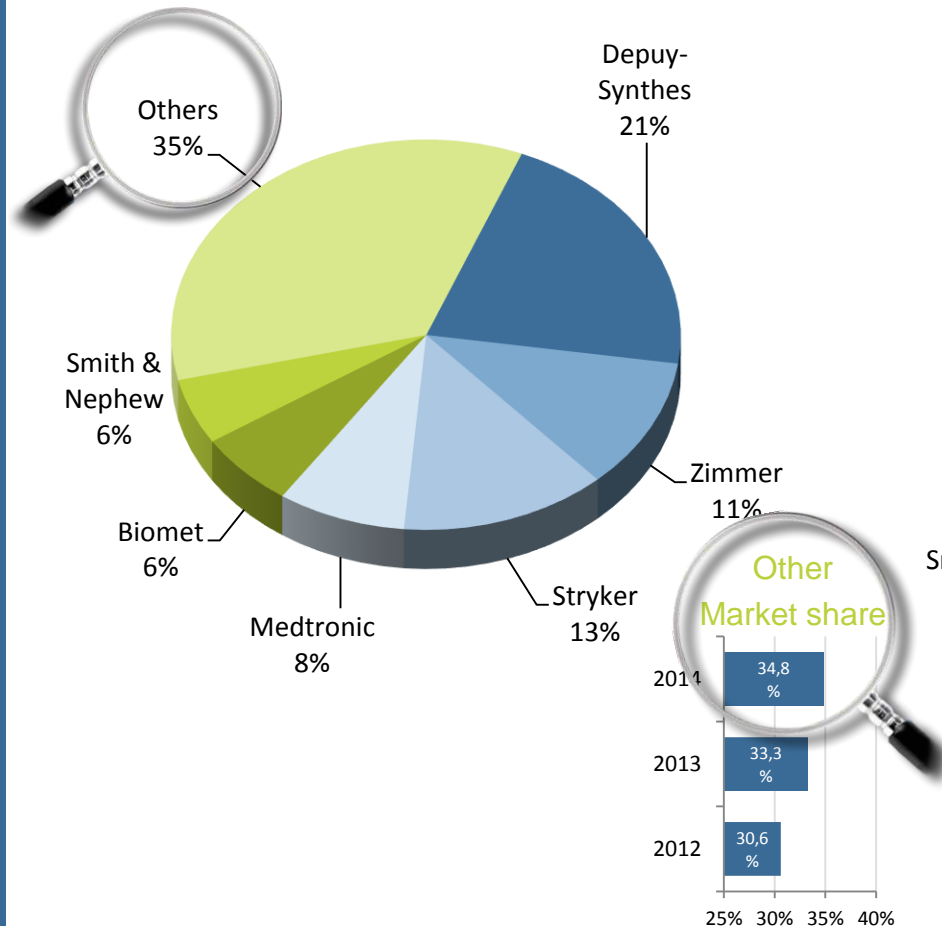
Market value (B\$)



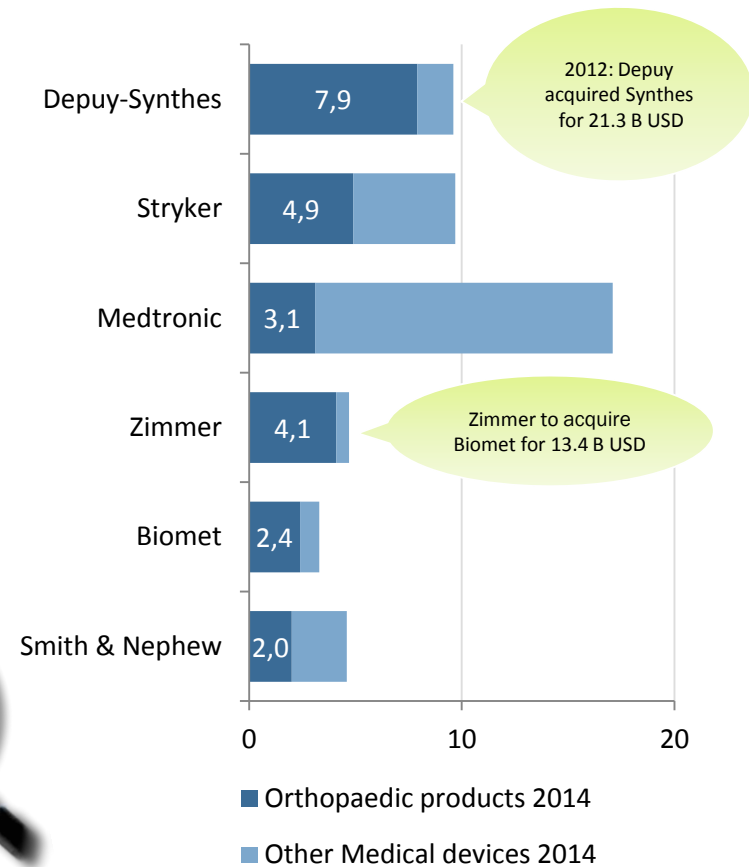
Source: Avicenne research & analysis 2015

Worldwide orthopaedic market in 2014: competition

2014 Worldwide Orthopaedic Market



2014 revenues of the Major Orthopaedic Companies (B\$)



Source: Avicenne research & analysis 2015

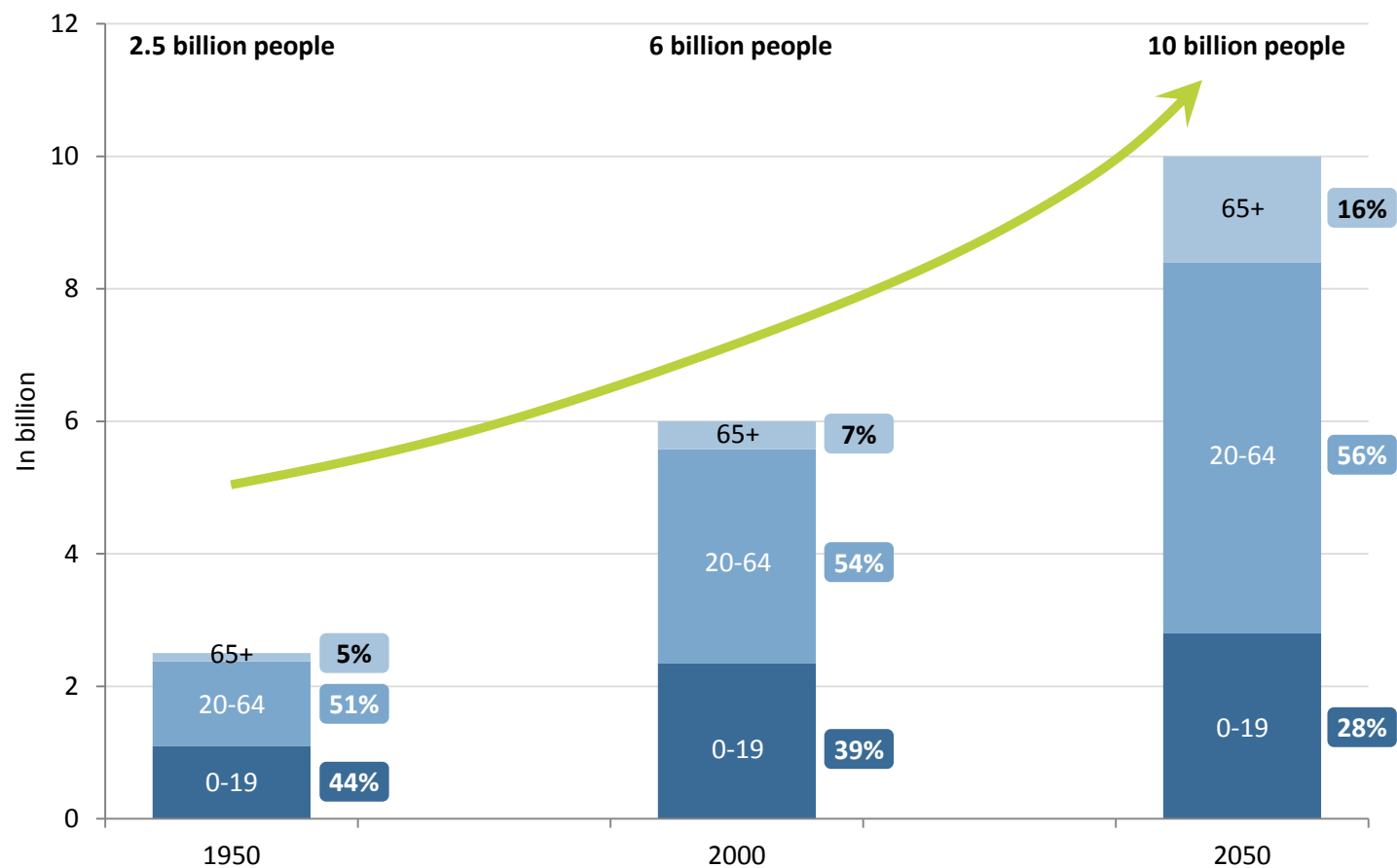
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Global population growth 1950-2050 and people over 65



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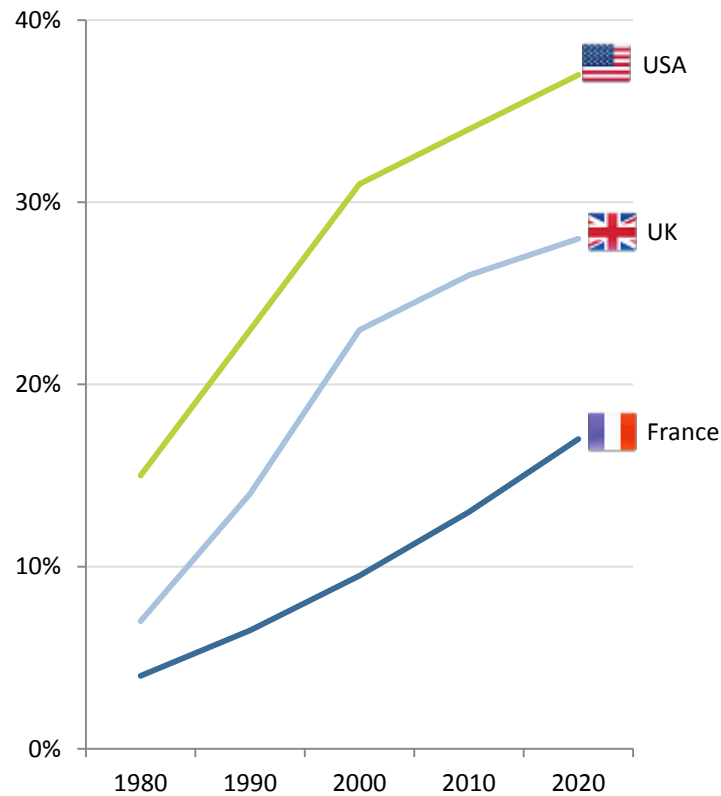
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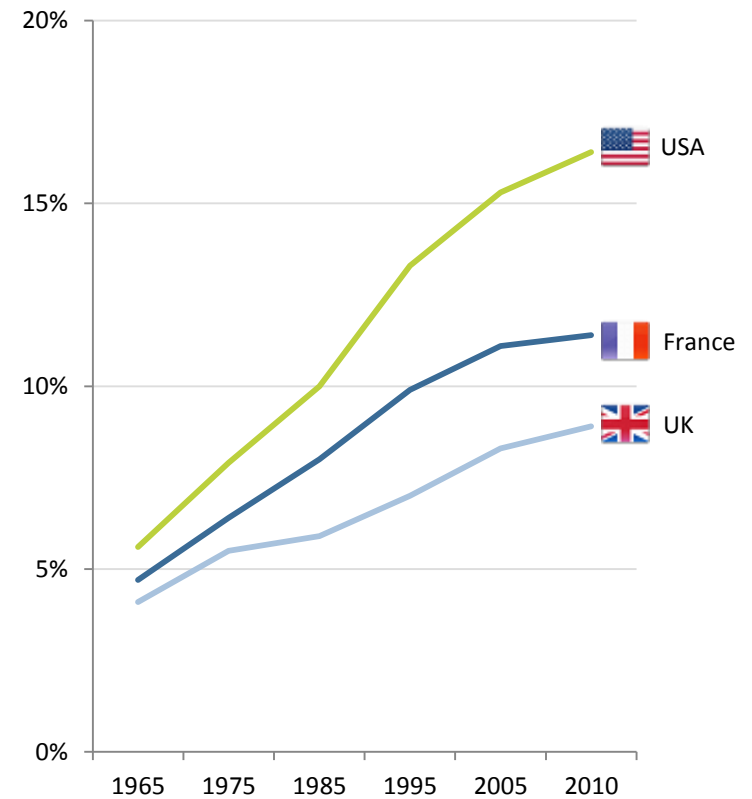
Source: United Nations – World Population Prospects, The 2012 Revision, Smith & Nephew annual report 2014

The market drivers: Demographic & Economic

Obesity in developing countries % of inhabitants

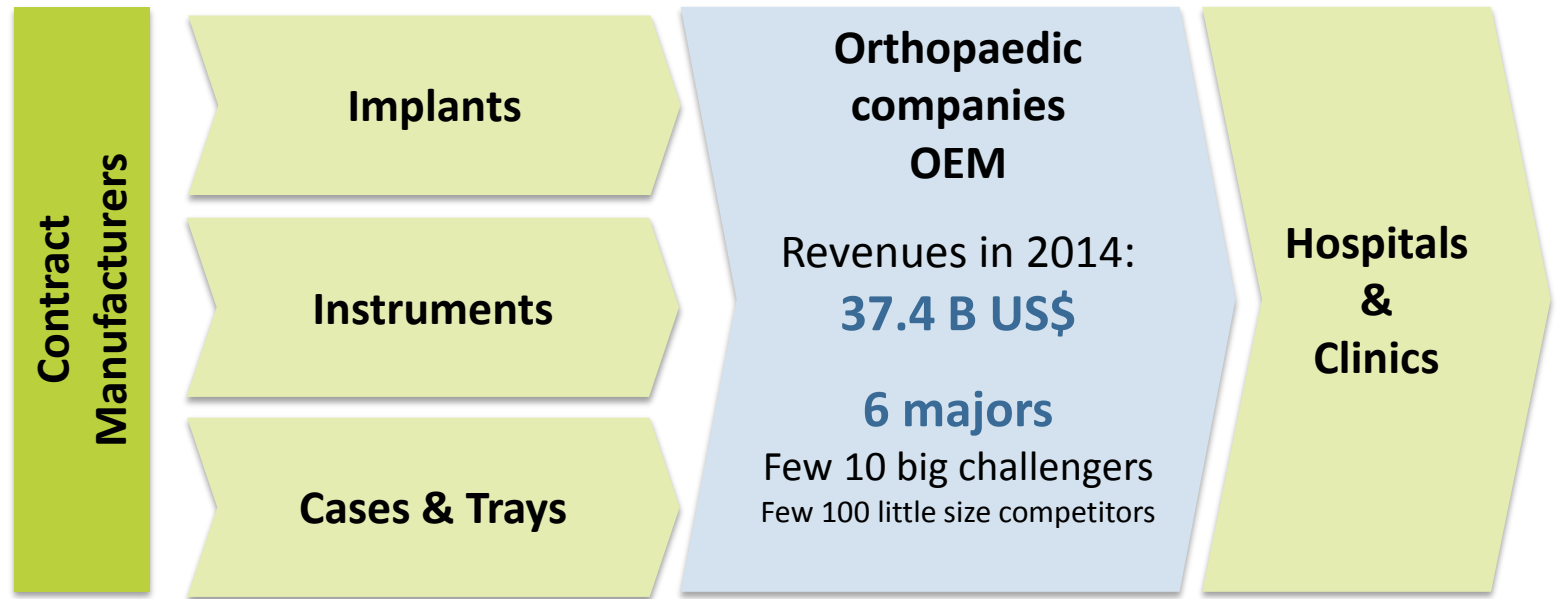


Health expenses % of GDP



Source : OCDE

Contract manufacturing market value chain



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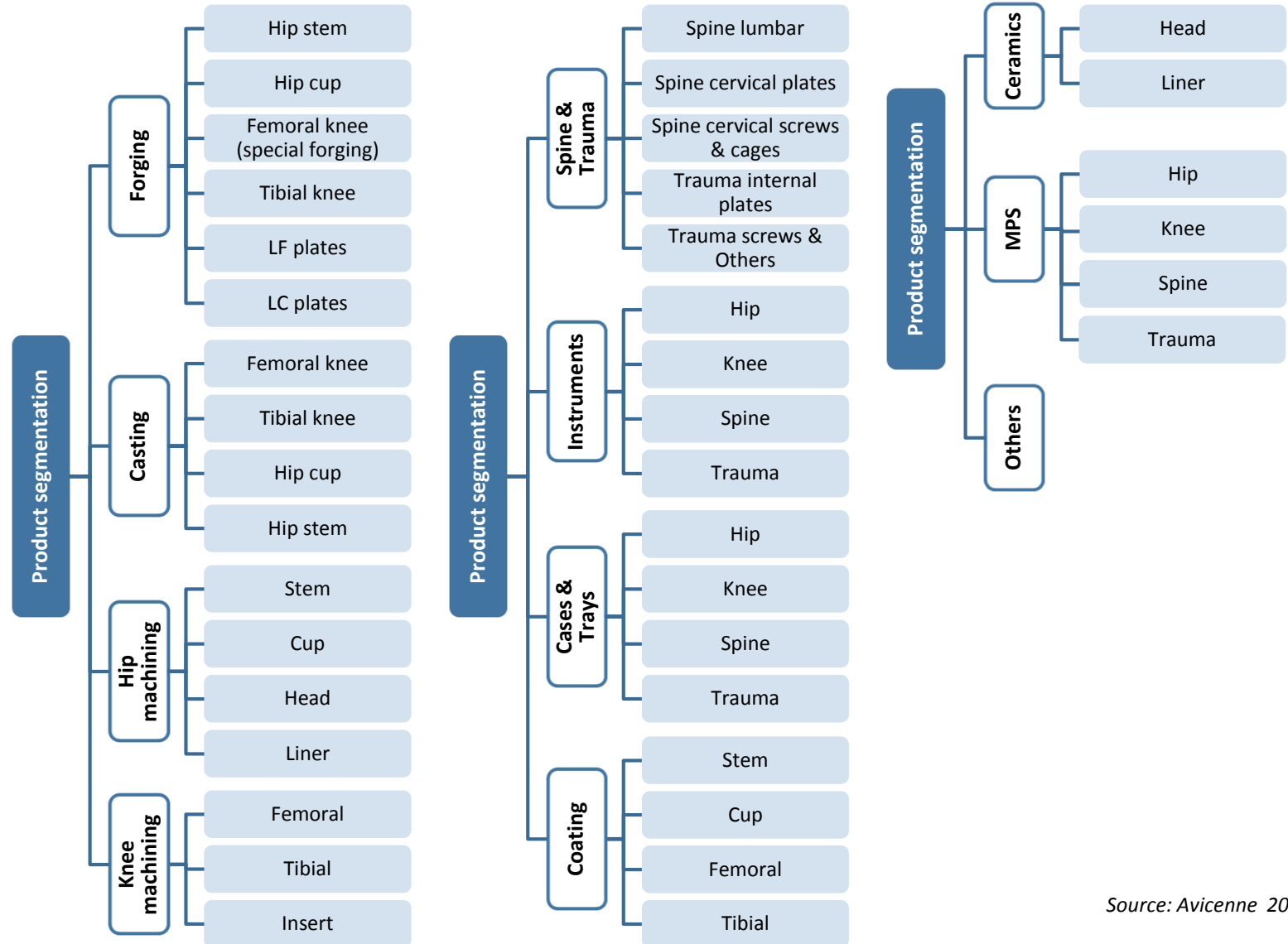
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Contract manufacturing product segmentation: 11 segments & 40 sub-segments



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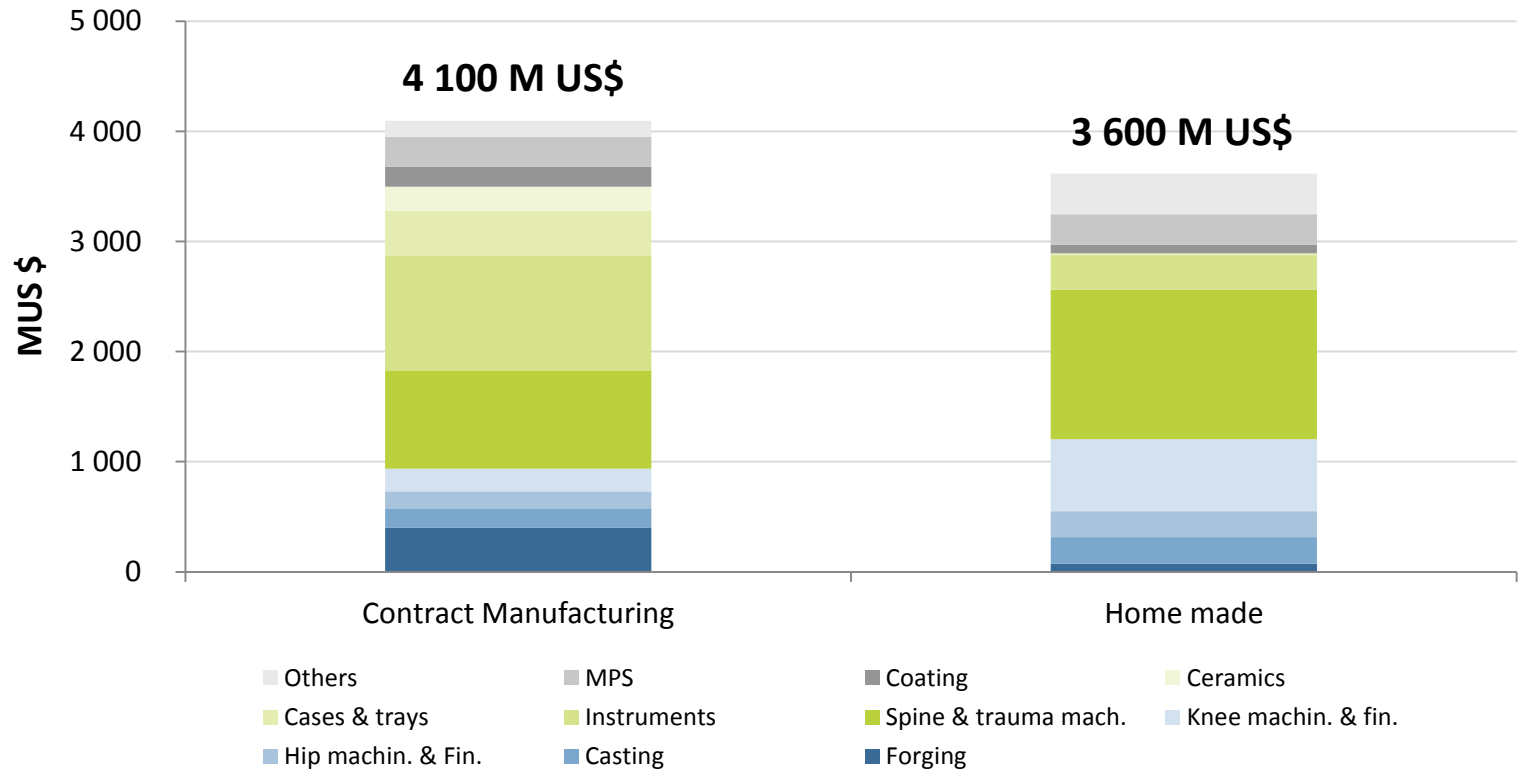
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Source: Avicenne 2015

Orthopaedic contract manufacturing & home-made in 2014 : 7,7 B US \$

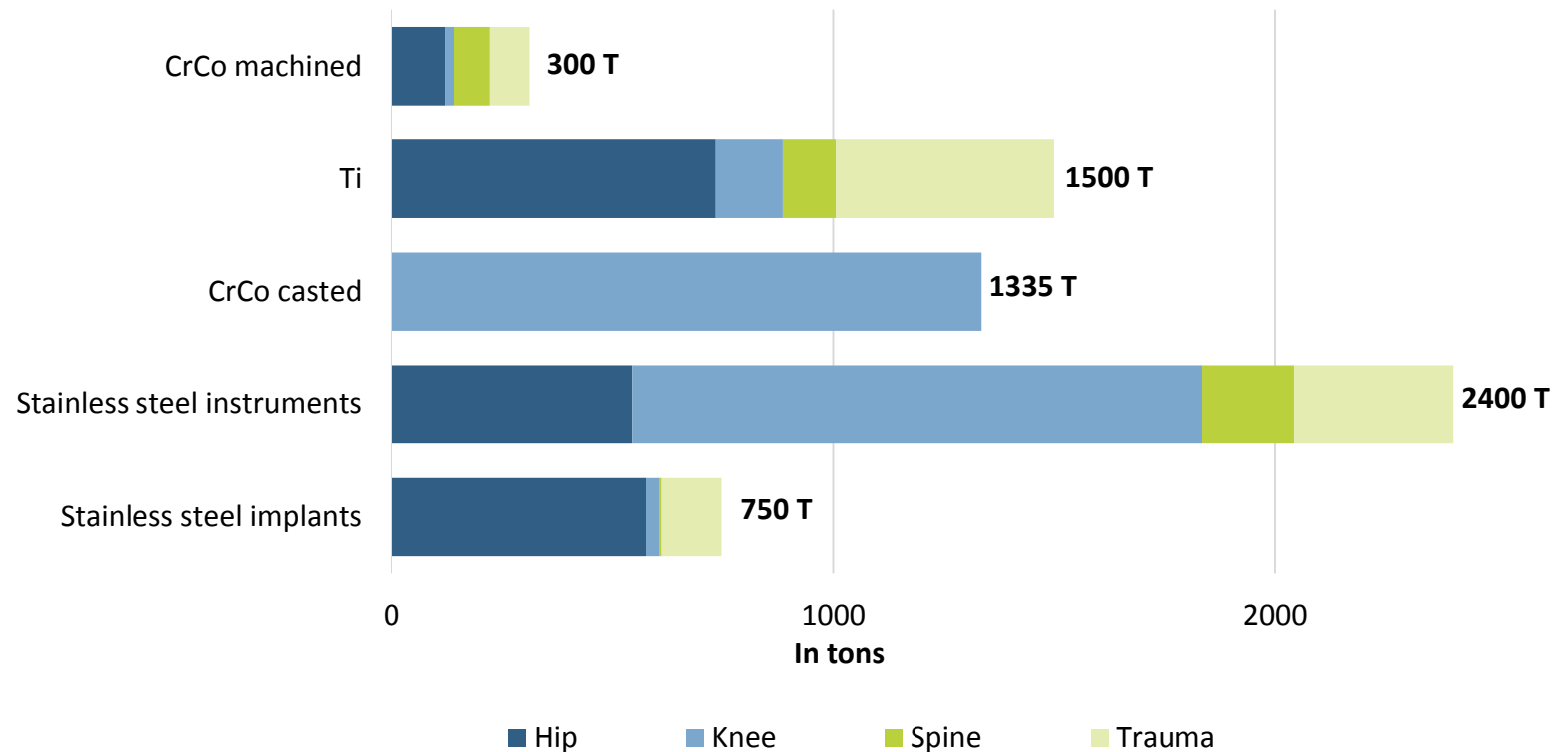


To manufacture the implants, instruments & other products, the OEMs in 2014 spent, 3.6 B US\$ in-house and paid their contract manufacturers 4.1 B US\$.

Source: Avicenne 2015

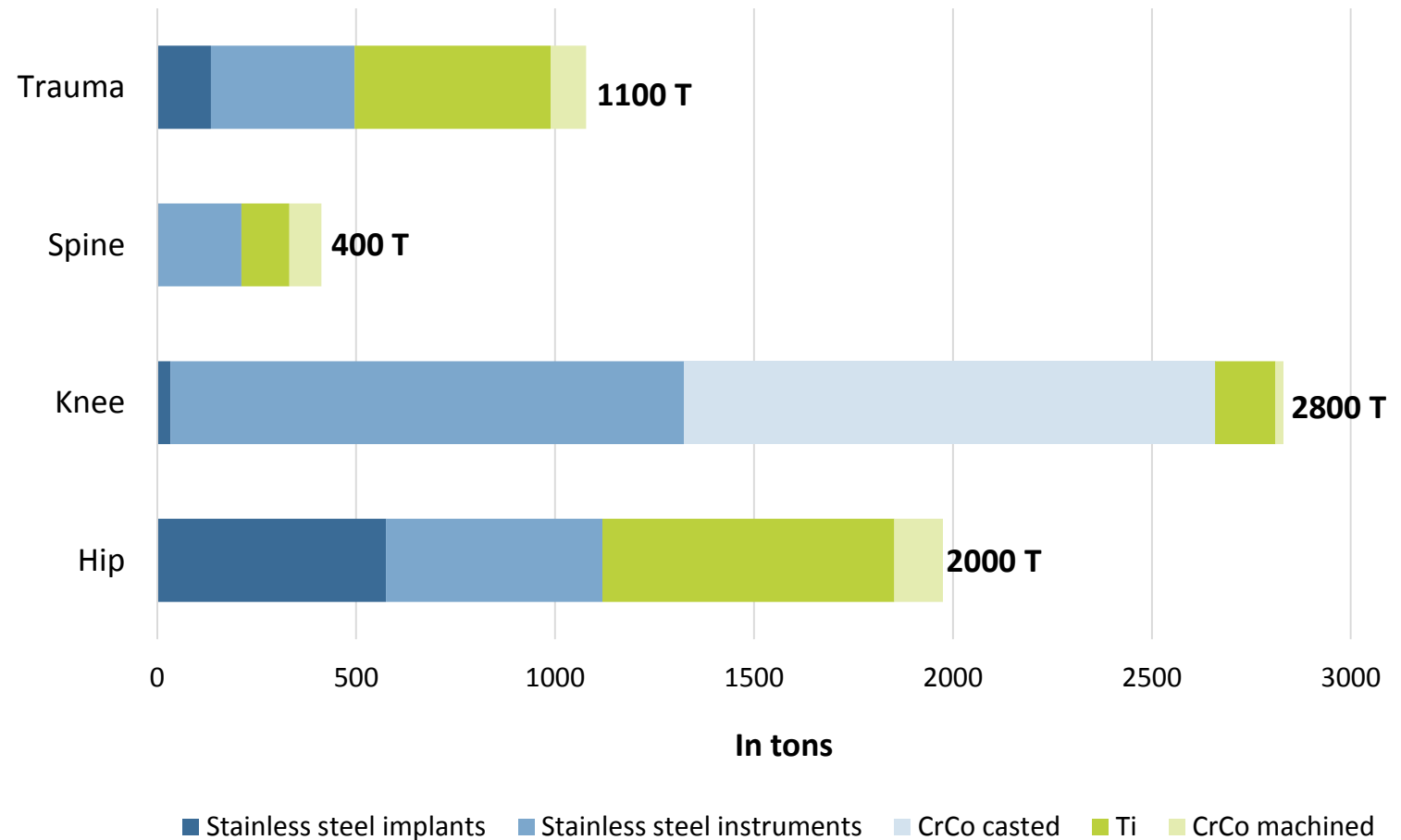
Volume of Raw Materials used in hip, knee, spine and trauma

Stainless steel is the most used material: 2 400 Tons to manufacture instruments & 750 Tons for implants. Titanium is used for 1 500 Tons.



Orthopaedic Raw Materials market in hip, knee, spine and trauma

Hip and knee represent 76% of the total raw materials needs



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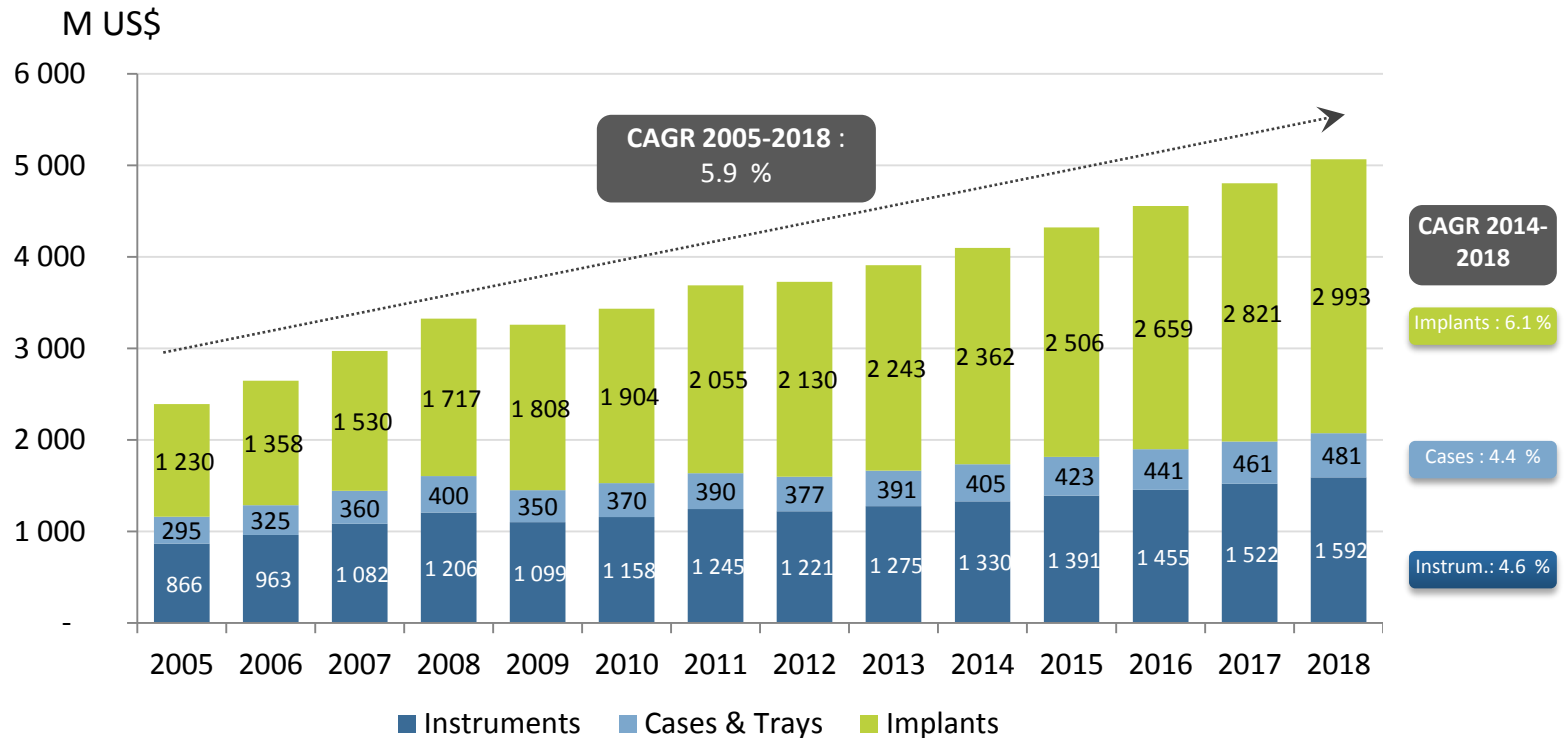
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Contract Manufacturing market historical revenues & forecasts (M US\$)

Implants will grow more rapidly than the instruments, cases & trays.



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Source: Avicenne research & analysis 2015

Additive Manufacturing history in Orthopaedics

Zimmer opened this market with Trabecular Metal, Lima & Adler, Italian based companies, started the mass market sales.

1997	2007	2008	2009	2011
<p>Zimmer used clinically Trabecular Metal based on the Tantalum Vapor Deposit Process for the hip cup</p>  <p>Source: Zimmer</p>	<p>Adler Ortho used its first Trabecular Titanium cup, Fixa Ti-Por</p>  <p>Source: Adler Ortho</p>	<p>109 Lima Delta TT cups were implanted between 2008-2011 in 98 patients</p>  <p>Source: Lima Corporate</p>	<p>Medtronic launched the FUSE Lumbar PLIF Cage</p>  <p>Source: Medtronic</p>	<p>Exactech, first implantation of its Intergrip porous metal acetabular - the first US company to offer FDA-cleared for EBM implants manufactured</p>  <p>Source: Exactech</p>

Customer main performances looking for:

- 🔗 Weight reduction (aero)
- 🔗 Advanced cooling (aero)
- 🔗 Bone ingrowth (implant)



Since 1997, Zimmer has used clinically the Trabecular Tantalum

Technology

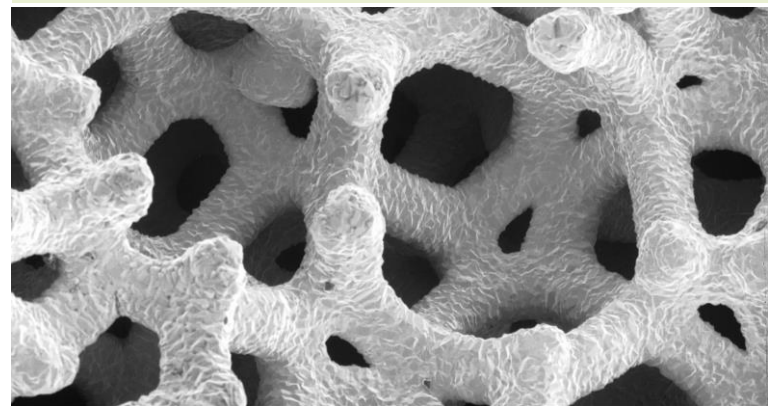


The precursor

ZIMMER

- 🕒 Technology: Trabecular Metal based on Tantalum Vapor deposit process
- 🕒 Issue: To accelerate the bone ingrowth process after the implant surgery
- 🕒 First Zimmer product targets : Revision hip cups
- 🕒 Pore size: 400 – 600 μm (Pore sizes of > 300 μm are required to support vascularization)

Trabecular is very attractive for the revision hip cup



Source: Zimmer

Story of Zimmer and Trabecular Tantalum

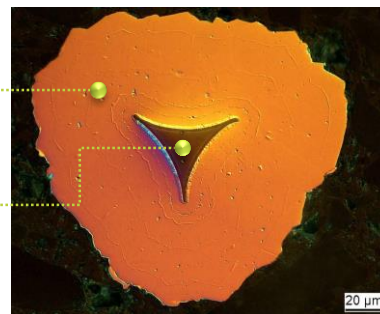
1997	2000	2004	2015
<ul style="list-style-type: none"> Zimmer started to use the Implex's Trabecular Metal Technology 	<ul style="list-style-type: none"> Zimmer entered into an exclusive worldwide strategic alliance for the marketing and sales of Implex's Trabecular Metal Technology 	<ul style="list-style-type: none"> Zimmer paid US\$ M 108 to acquire Implex and created the Zimmer Trabecular Metal Technology Division 	<ul style="list-style-type: none"> The Trabecular Metal is massively used by Zimmer for certain products and certain areas: shoulder, dental, hip cup,....

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Tantalum

Vitreous Carbon



Source : Zimmer
<https://zimmerbiomet.tv/channels/41>



Source : Zimmer, Parsippany, New Jersey facility

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Zimmer, Trabecular Metal related implants

Related products

Zimmer Trabecular Metal™ Patella



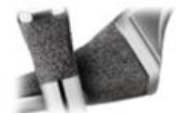
Zimmer Trabecular Metal CR/LPS Monoblock Tibia



Zimmer Trabecular Metal™ Femoral and Tibial Cone Augments



Trabecular Metal Primary Hip Prosthesis



Trabecular Metal Acetabular Revision system



Continuum Acetabular System



Trabecular Metal™ Modular Acetabular System



Zimmer Trabecular Metal™ Glenoid Fixation

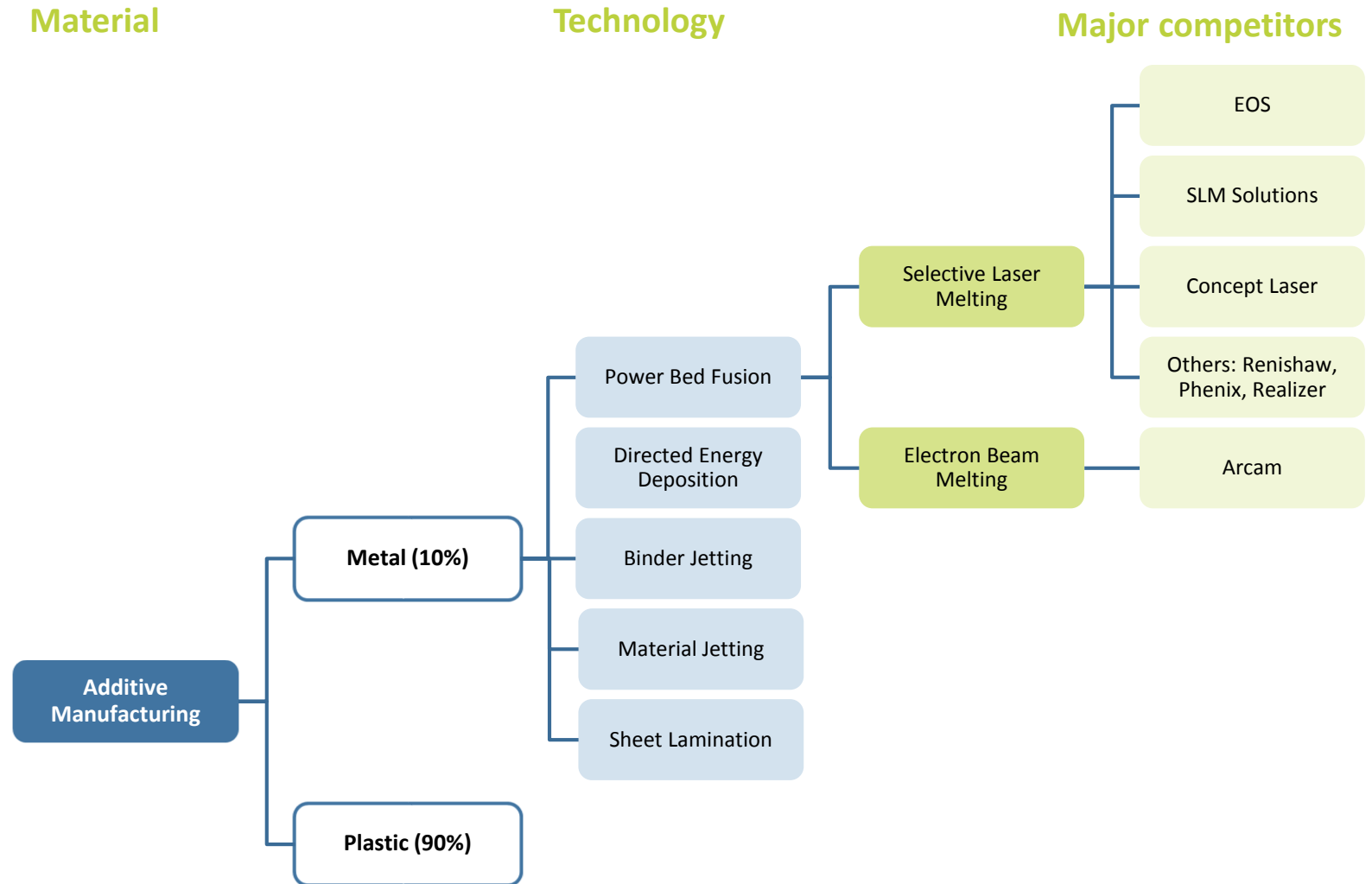


Zimmer Trabecular Metal™ reverse Shoulder System



Blood enters pores = catalyst for bone ingrowth

Metal Additive Manufacturing: Technologies and major competitors



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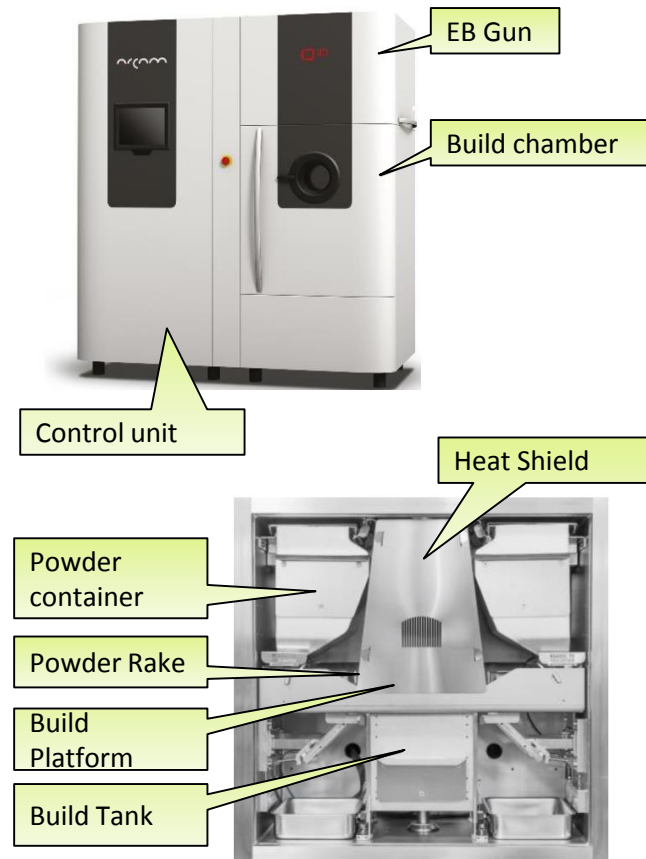
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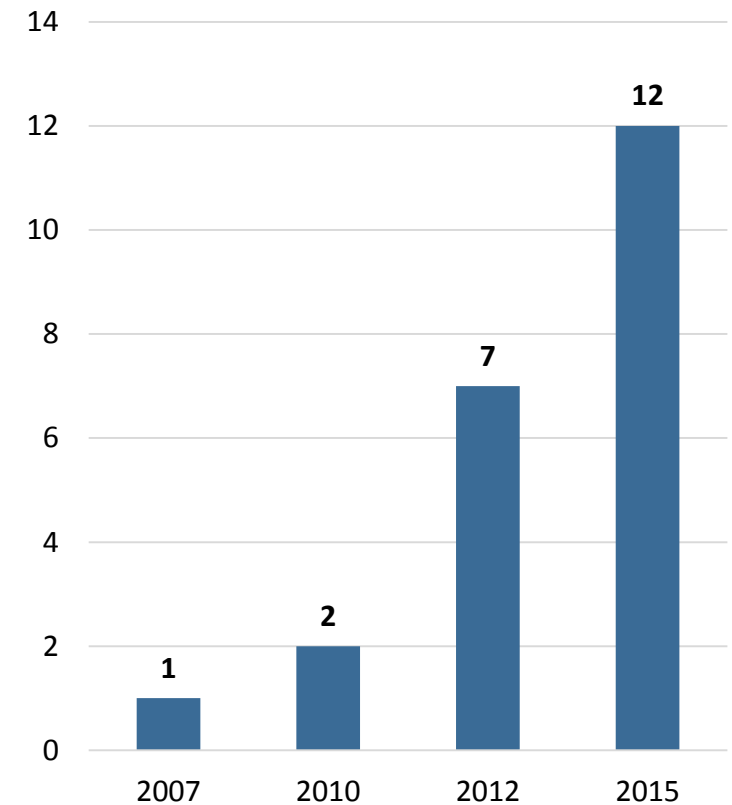
Arcam with ~ 60 EBM installed base for orthopaedic industry

The EBM® Machine CAD TO METAL® Arcam AB



Arcam EBM machines, source: Arcam 2015

LIMA EBM Installed base



Source: Avicenne Research & Analysis 2015

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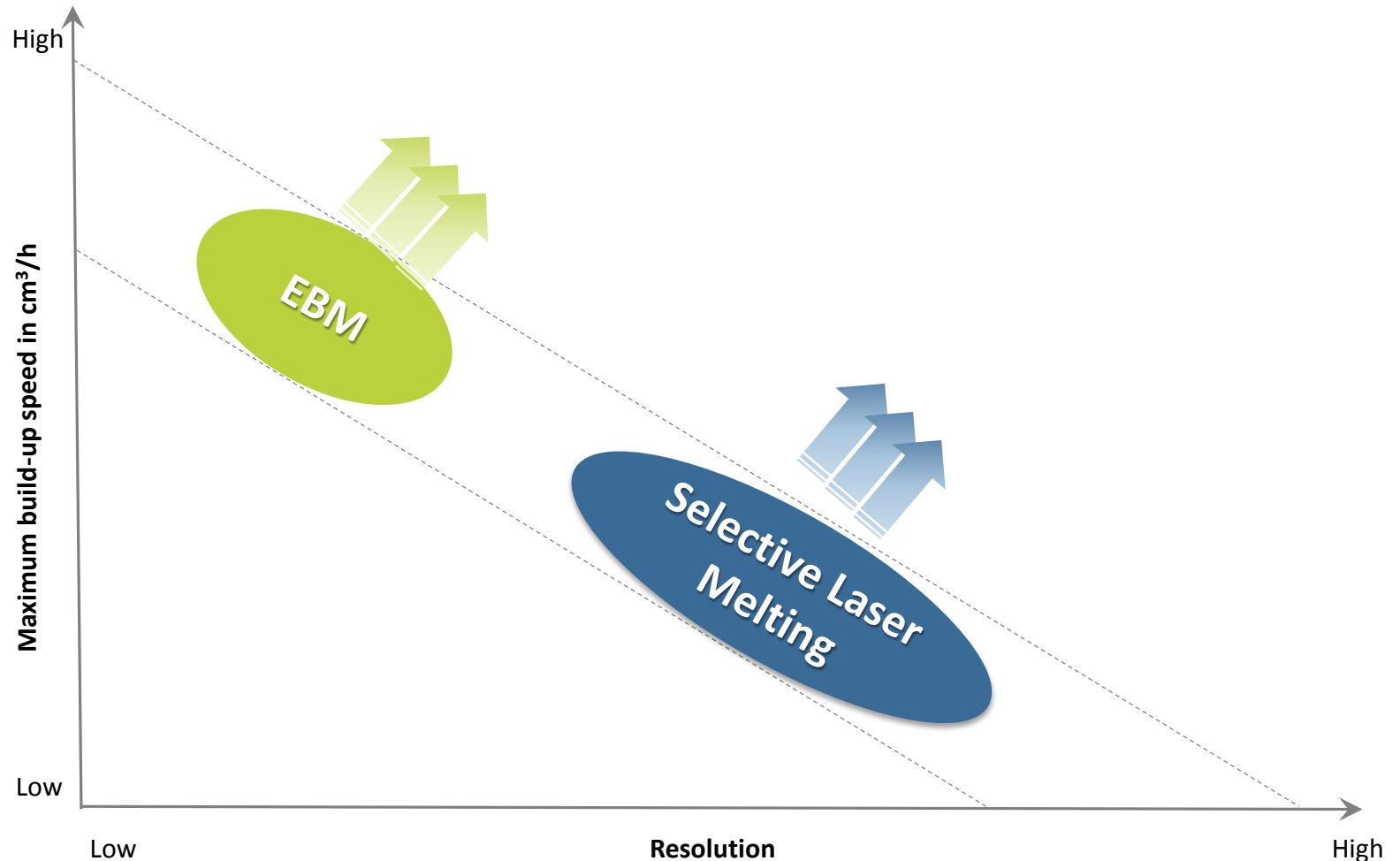
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Illustrative build-up speed and resolution of selected Metal Additive Manufacturing systems



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Depuy Spine uses Additive Manufacturing for prototyping of complex surgical tools



*EOSINT M 270 used by
Depuy Spine*

source: EOS



Prototype of an Expedium SFX Cross Connector measuring device, which measures the distance between rods to indicate the size implant to use

Source: DePuy Spine



Prototype of a Plate Bender, used to contour plates for spinal surgery

Source: DePuy Spine, Raynham, MA (USA)

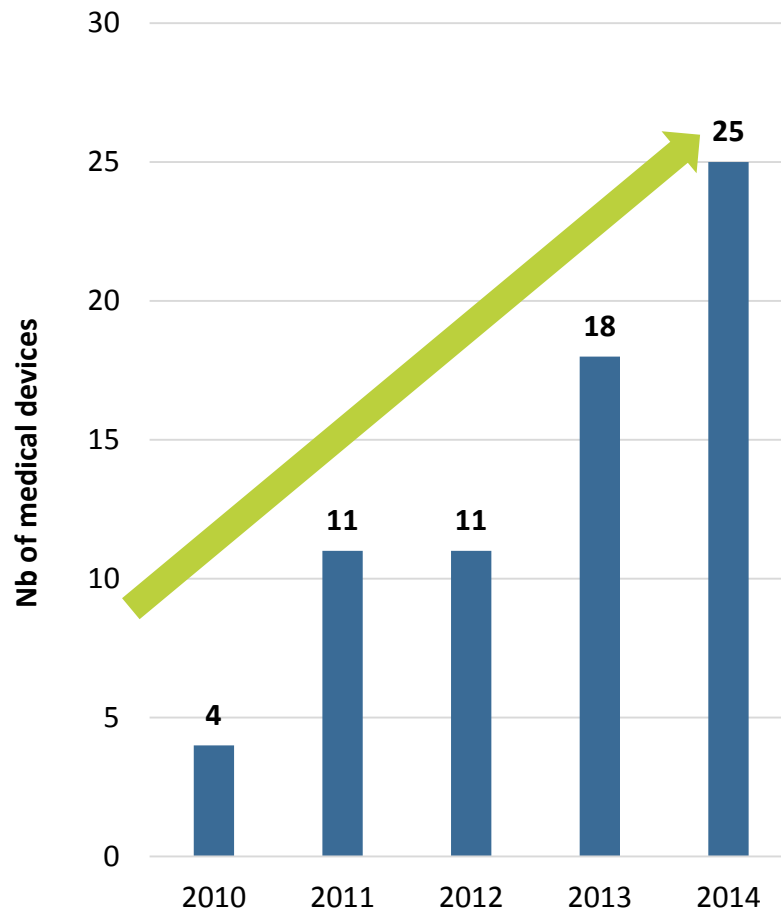
Smith & Nephew uses Additive Manufacturing for customized cutting blocks

Using the patient's MRI and X-Ray, Smith & Nephew creates customized cutting blocks that will eliminate up to 22 surgical steps from the conventional surgical procedure. With multiple implant options the patient-matched cutting blocks utilize the mechanical axis for alignment, potentially leading to greater implant longevity.



*Smith & Nephew VISIONAIRE Patient Matched Cutting Blocks
Made by EOS machine, Source: Smith & Nephew*

FDA clearance for medical devices using Additive Manufacturing in USA



Source: Laura Ricles, FDA Commissioner's fellow



iTotal® TKR by ConforMIS

http://www.accessdata.fda.gov/cdrh_docs/pdf12/K122870.pdf



Cup by Medical Modeling





http://www.accessdata.fda.gov/cdrh_docs/pdf12/K120956.pdf



Novation Crown, Exactech

http://www.accessdata.fda.gov/cdrh_docs/pdf10/K102975.pdf

Number of implants produced using Additive Manufacturing

	Nb of implants (excluding dental) in 2014	Rationals
	Several 10 000 / year <i>Source: Avicenne Research & Analysis 2015</i>	50% of Zimmer shoulders sales come from reversed, anatomic and revision trabecular metal products
	25 000 implants (2010-2014) <i>Source: C. Dottino in Implants 2014</i>	More than 3 EBM machines installed
	Several 10 000 cups/year <i>Source: Avicenne Research & Analysis 2015,</i>	More than 10 EBM machines are installed
	Several 1 000 or 10 000 ?	First company to obtain FDA clearance in USA

Source: Avicenne Research & Analysis 2015

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Source: Zimmer



Source: Lima Corporate



Source: Lima Corporate



Source: Exactech

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Equipment suppliers for Orthopaedics



**Orthopaedic
Installed
base
2015**



Source: Arcam



Source: EOS

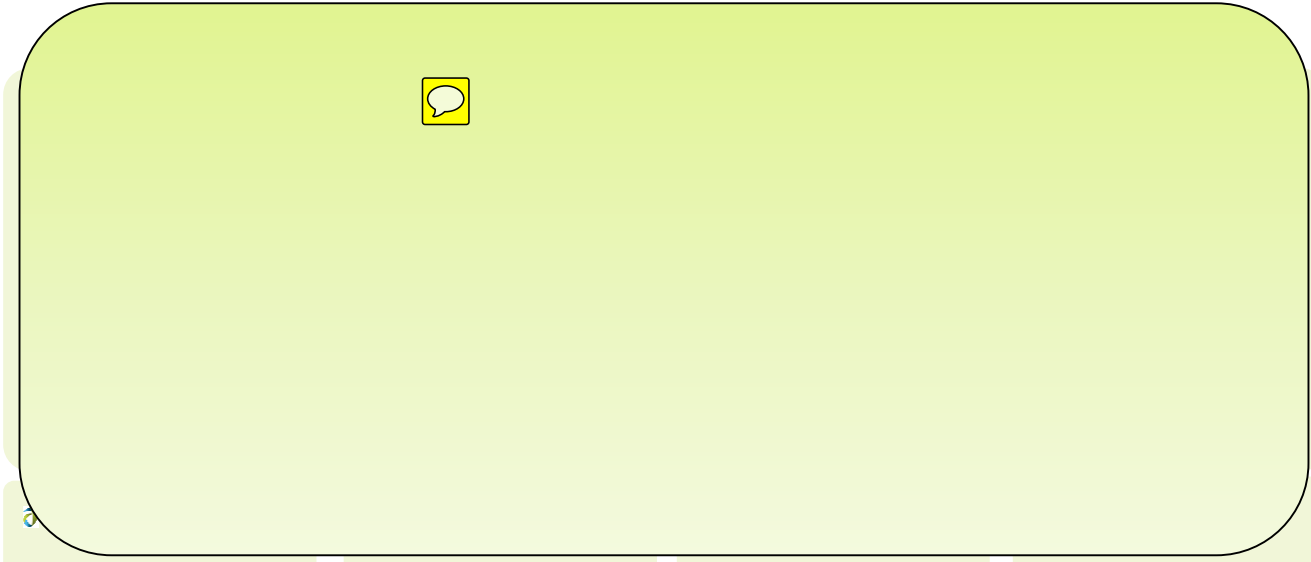


Source: Concept Laser



Source: SLM Solutions

Customers



**Estimated
Metal Install.
base in 2014**

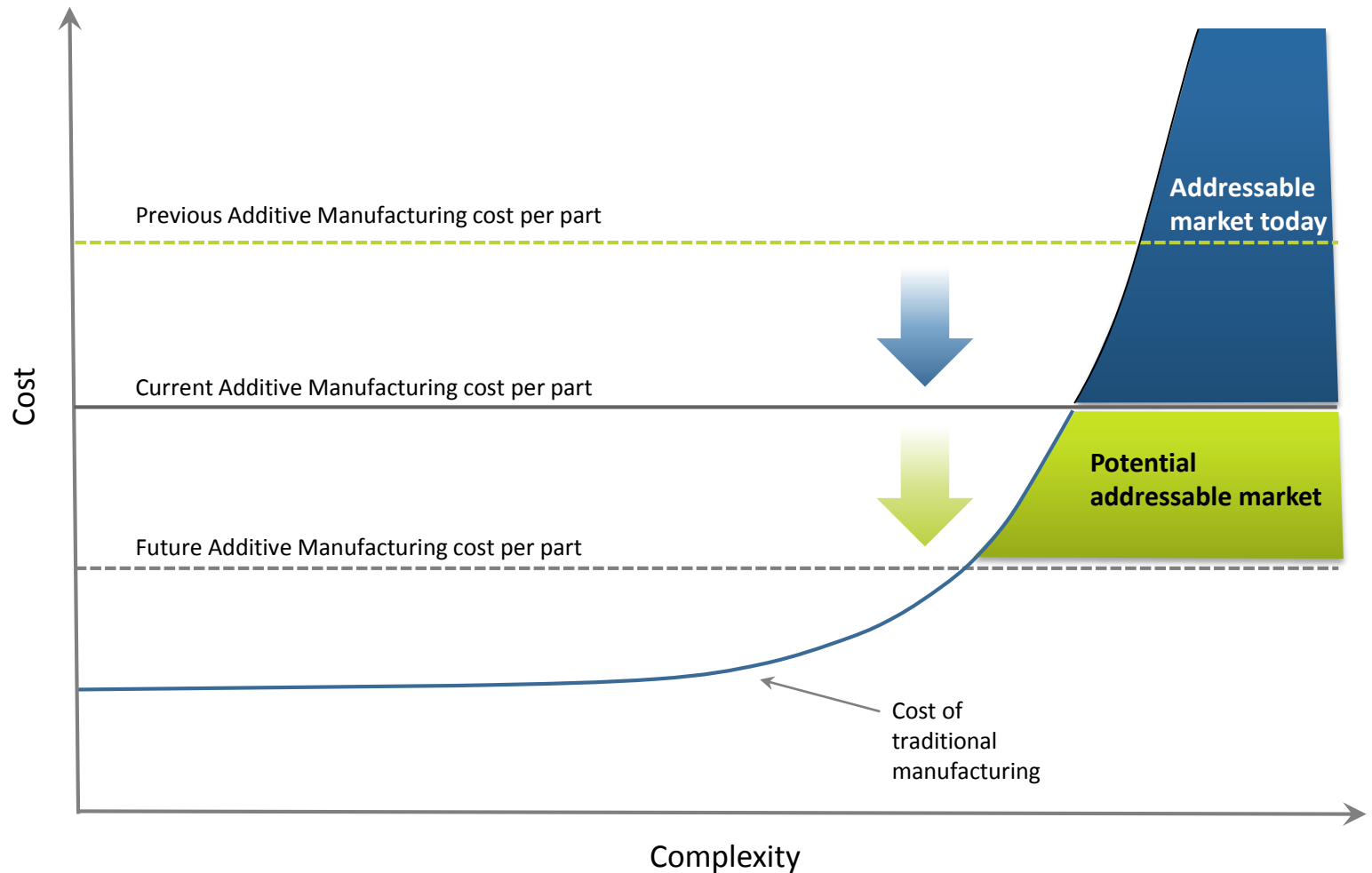
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Addressable market should increase with lower Additive Manufacturing cost



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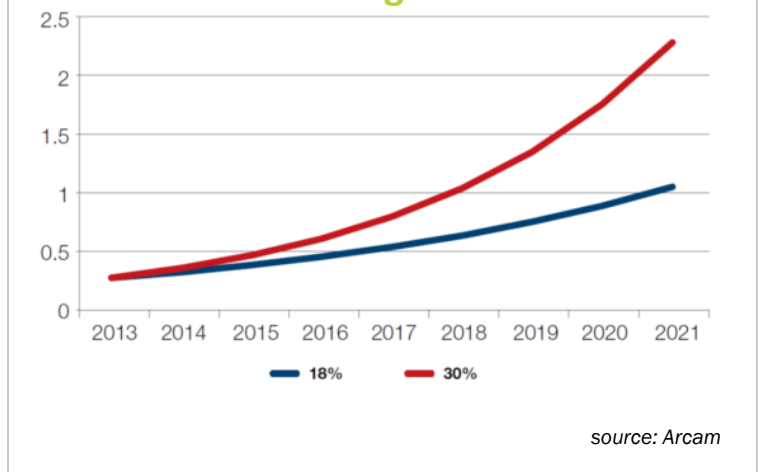
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Take home messages

- 🕒 Additive Manufacturing is now a mature technology used for more than 15 years in the orthopaedic industry.
- 🕒 Additive Manufacturing enables the manufacture of complex metal parts, simultaneously and for different sizes, shapes and design.
- 🕒 Zimmer, one of the Major orthopaedic companies, penetrated this market 15 years ago with a proprietary technology acquired from IMPLEX, thereby opening the trabecular structure market with an investment of several hundred million US\$.
- 🕒 Italy for Additive Manufacturing is the most advanced market: Challengers like Lima Corporate and Adler Ortho have invested massively in this technology, following Zimmer, the historical player. The main trabecular products are hip cups, sold by several thousands in Italy each year, and followed by other products like shoulder implants, knee tibial plates, mini-hip stems, etc...
- 🕒 Equipment suppliers like EOS & Arcam have 20 years experience in machines, CAD software, powder and in the technology.
- 🕒 STRYKER, another Major orthopaedic company, have received 510(k) clearance for a few orthopedic implants made using Additive Manufacturing. In 2014, almost 25 orthopaedic products, made by Additive Manufacturing had received 510(k) clearance, in the USA.
- 🕒 Today, if the orthopaedic industry use around 1 500 tons of Titanium per year, Additive Manufacturing uses less than 50 tons of titanium per year for Orthopaedic purposes. (< 3% of the total).
- 🕒 Today Lima Corporate needs 2 Tons of Titanium for AM per year and Adler Ortho needs 0.7 Tons/y.
- 🕒 CMF implants will also be massively produced by AM due to their complex profiles and small dimensions.
- 🕒 The market growth 2013-2021 for the Additive Manufacturing in Metal, will be between 18% and 30%, according to several industry forecasts. Orthopaedic applications will be one of most dynamic segments.

Market growth 2013-2021 in USD billion for metal AM with 18 to 30 percent annual growth



Appendixes

Additive and Trabecular Manufacturing
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Ali MADANI
Chief Executive
Officer of
AVICENNE

- Ali founded AVICENNE in 1992. He holds a Science degree from Université Paris Sud Orsay and École Normale Supérieure de Cachan, followed by a MBA in Innovation Management from Paris Dauphine University.
- Since 1990 he has been working on strategic and marketing studies in the medical sector. He has advised major players in this industry (Medtronic, Stryker, Zimmer, Depuy,...) in terms of strategy development and implementation, technical and economic appraisals and mergers and acquisitions. He has also advised multiple Private Equities firms for acquisitions (> € 50M value) and build-up. He has been involved for the mid-size companies in the entry strategies for new markets, adjacencies or new geographic territories and also business model improvements and partnership strategies.
- Globally, he has been involved in more than 300 projects for 100+ customers in the Medical Devices Industry.
- Ali has published several annual surveys like “European orthopaedic Market 2013-2018” or “Worldwide orthopaedic contract manufacturing market 2014-2018 and top 100 supplier profiles» and he is speaker and chairman of several medical device conferences worldwide.
- In 2005, he founded “IMPLANTS” a medical device industry conference and exhibition, which he presides ever since. Ali is fluent in French & English.