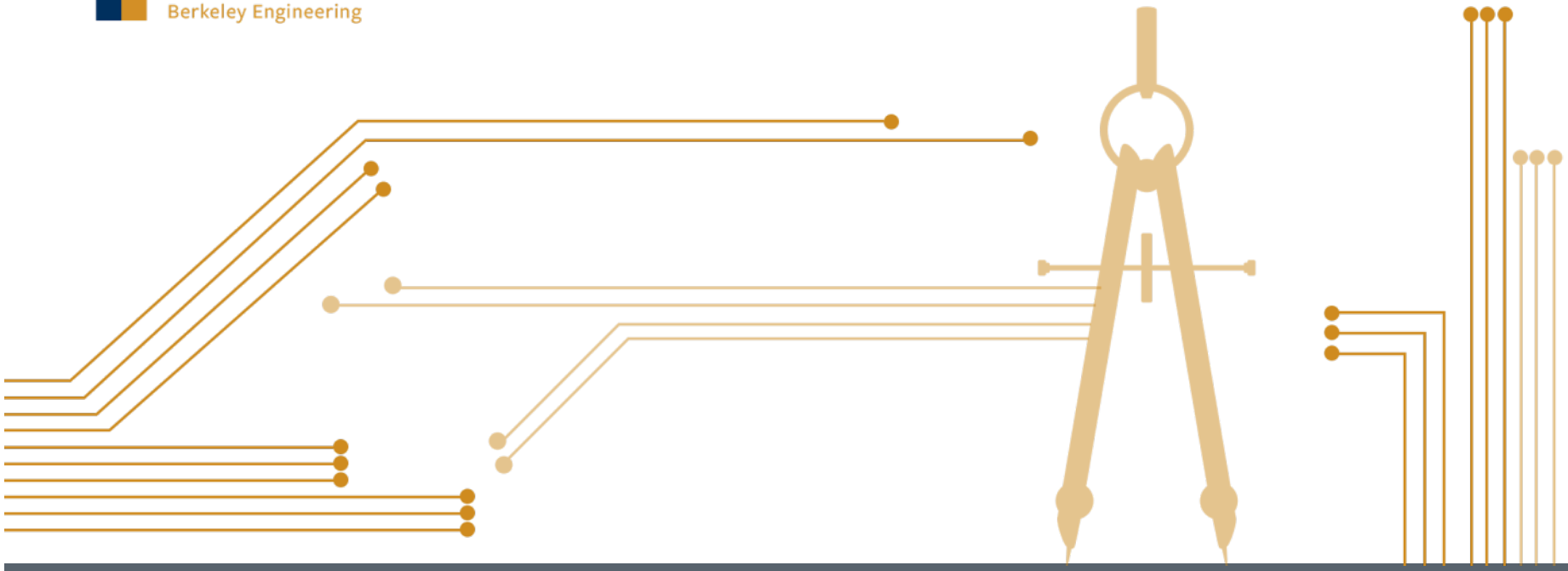
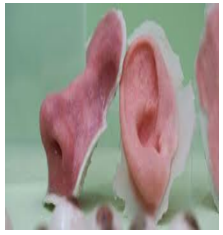


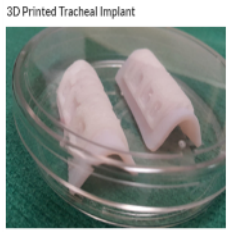
Disruptive Medicine Using 3D Printing

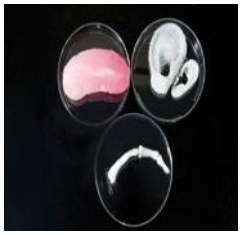
Jeff Hudgens, Naveen Kini, Madhukar Korupolu, Joung Lee, Eric Ng, Yang Seok Ki.

3D Printing for Medical Applications



Uniquely Yours!





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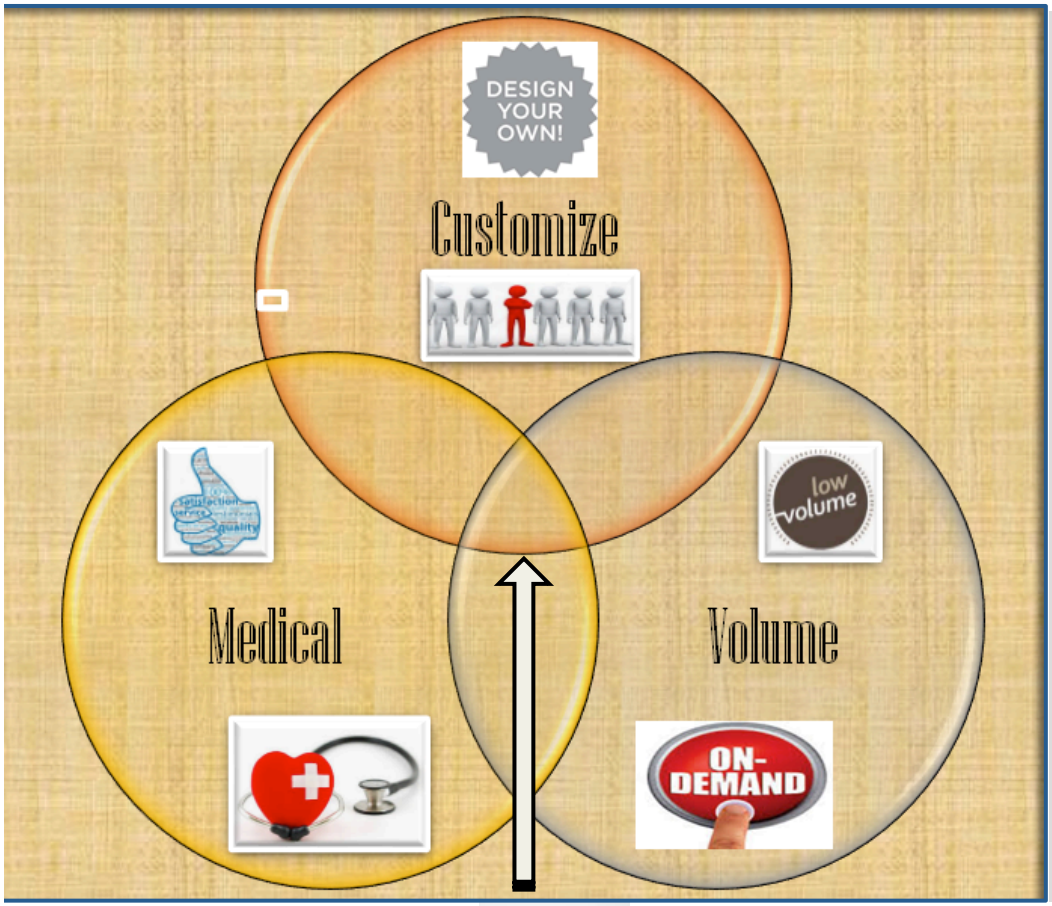
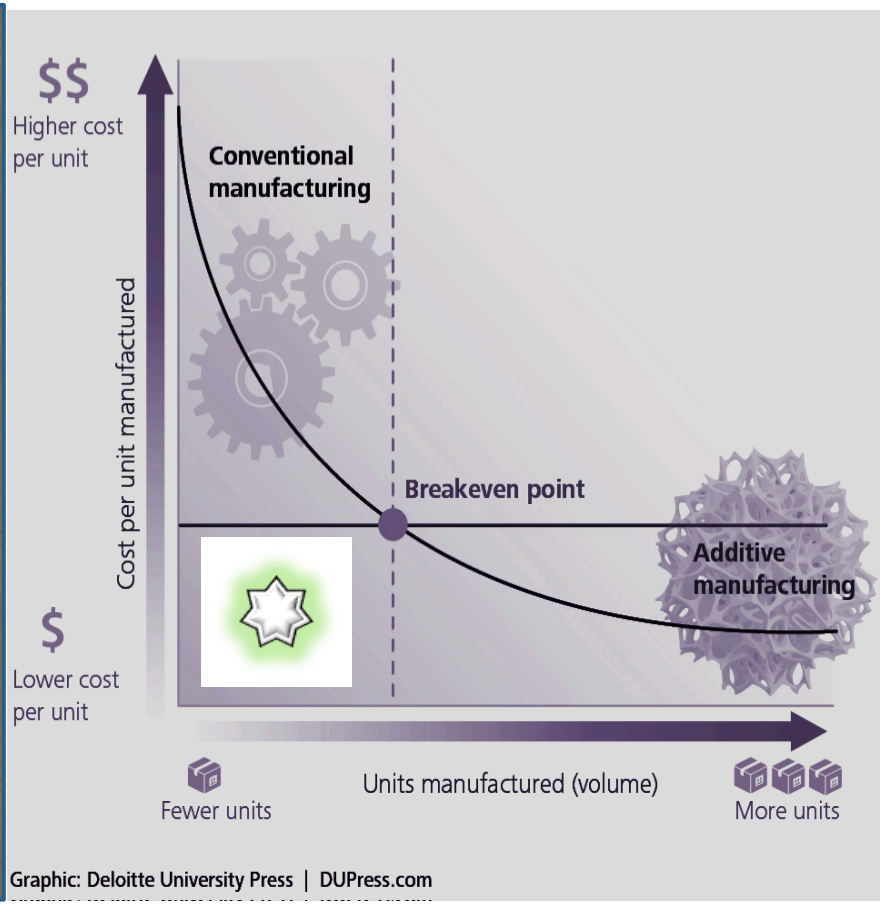
Value Proposition
(3D Printing in Medicine)





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Hype versus Reality

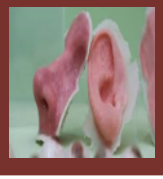
Organ

Knee and Hip Replacement

Cranium Replacement

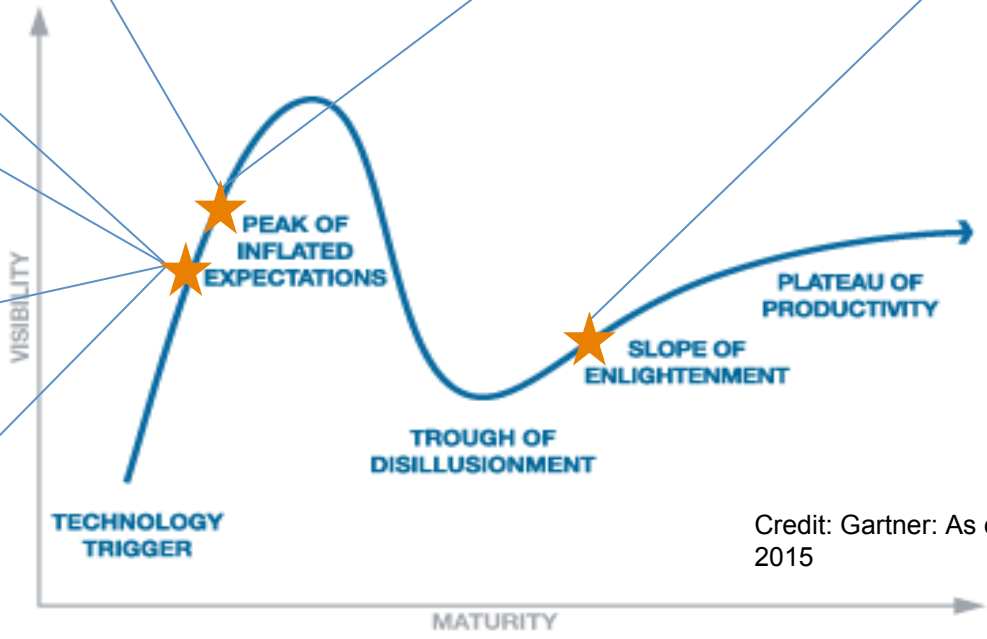
Dental Solution

Ear & Spinal Cartilage



Synthetic Skin

Bone



Credit: Gartner: As of July 2015

Gartner's hype cycle: True disruption has to show viability through productivity

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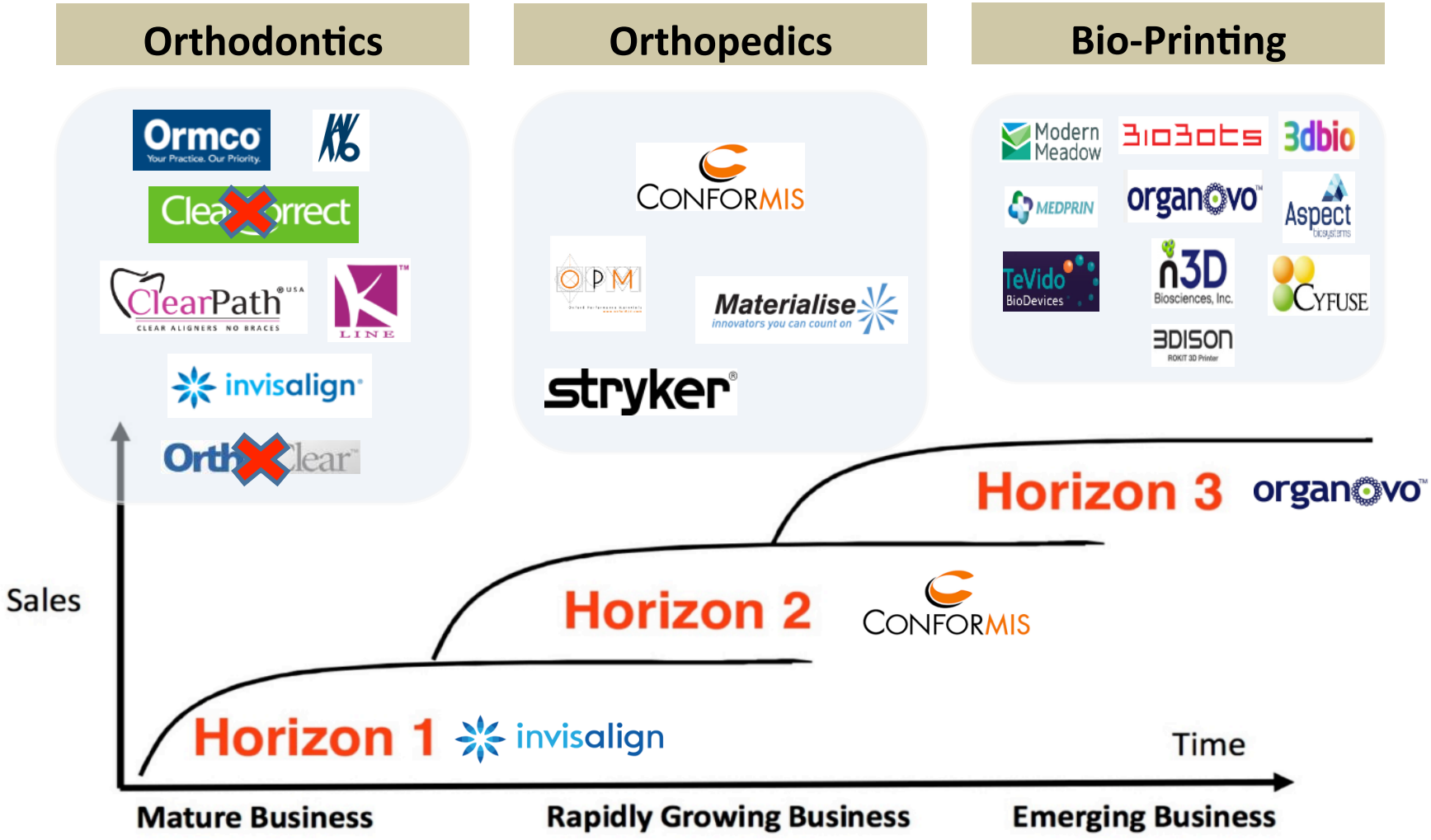
Horizon of Innovation



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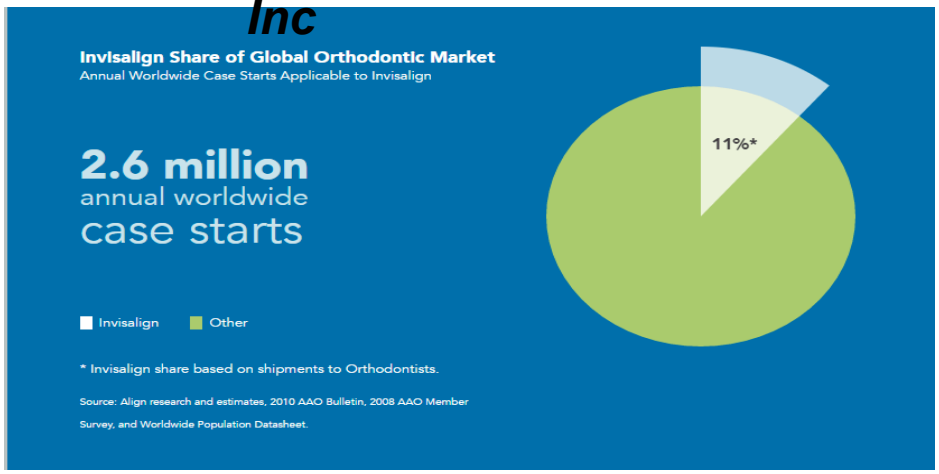
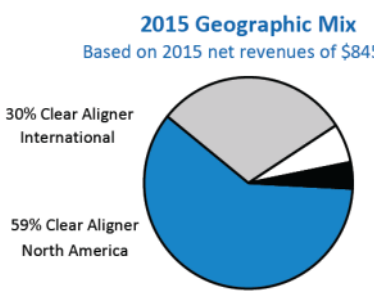
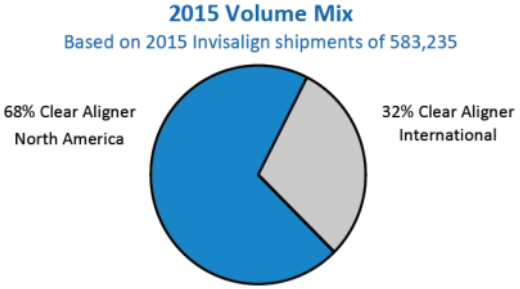
Horizon #1 : Orthodontic Treatment for Malocclusion

- **Accelerating consumer acceptance :**
  - **44k** patients from 1999-2002
  - **286k** patients/yr in 2015
    - 11% of SAM.
- **Key Growth Milestones :**
  - 1998 FDA Approval
    - Invisalign Adult Full
  - 2001 IPO; Int'l expansion begins
  - 2008 Product Expansion continues
    - Invisalign Teen
    - Invisalign Assist
      - Non-orthodontic GP/dentists
  - 2011 Inorganic growth
    - Aquires iTero Scanner
  - 2015 - 3M total patients treated
  - **2017 - Key Patents Expire**
    - ***Key threat of deep-pocketed competition begins (3M, Dentsply, Ormco, …)***

Align Technologies, Inc







Industry Landscape

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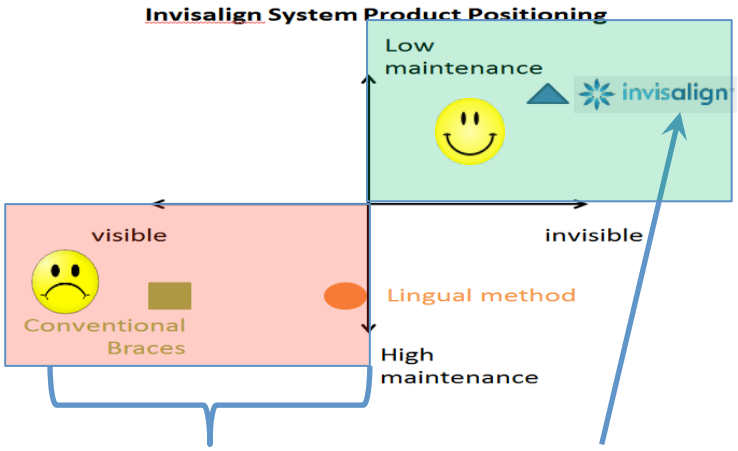
Align Technology's Story of Disruption



Invisalign® is a differentiated, IP-protected treatment solution taking MS from the conventional bracket and wire hardware suppliers

- Conventional braces require frequent office visits for adjustments
  - ➢ Invisalign is a progressive pkg of aligners - patient switches sequentially every 3 weeks (at home)

Disruption: *Service providers have less 'chair time' and more patients ($$'s)*

Disruption: *Consumers prefer the aesthetics and and low maintenance of the removable aligners v. wire braces*

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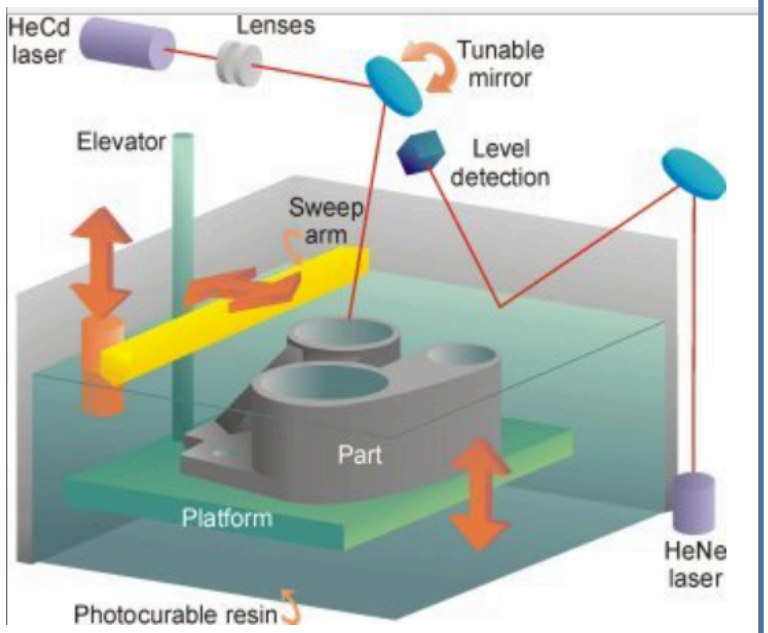
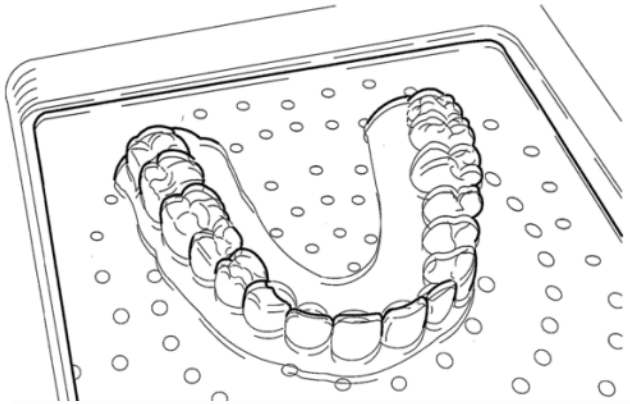
Align's 3D Printing Technology Formula for Success



3D Systems Printer

1) **SERVICE model using 3D printing equipment**
2) **Exclusive partnership agreement with 3D Systems (DDD)**
3) **Proprietary overmold materials (differentiation)**
4) **Early buy-in of Orthodontists (customer acceptance)**
5) **In-house treatment algorithm (expertise)**
6) **Expansion to GP/Dentists with in-house guidance**



Overmolded and cured Invisalign®

- 3D makes 10-20 progressive treatment molds
- Algorithms determine the preliminary plan
- Orthodontist confirms plan

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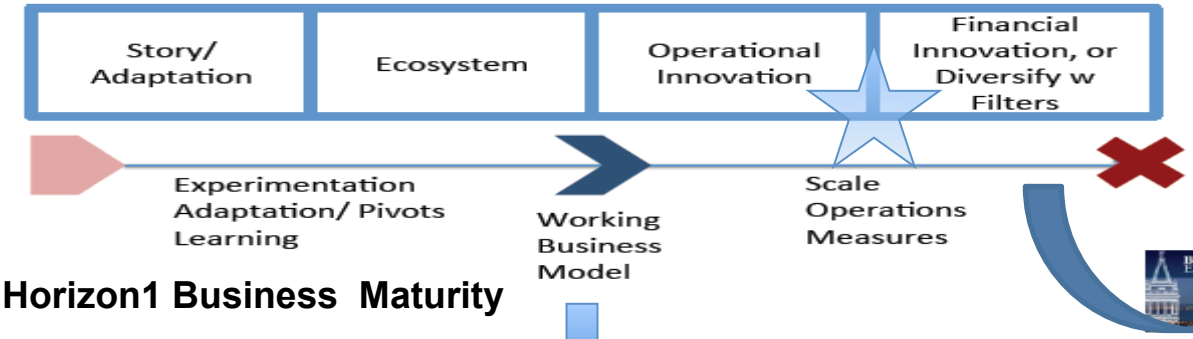
Align: The Pursuit of Certainty



Suppliers

Regulators

Competition

Customer

ECOSYSTEM

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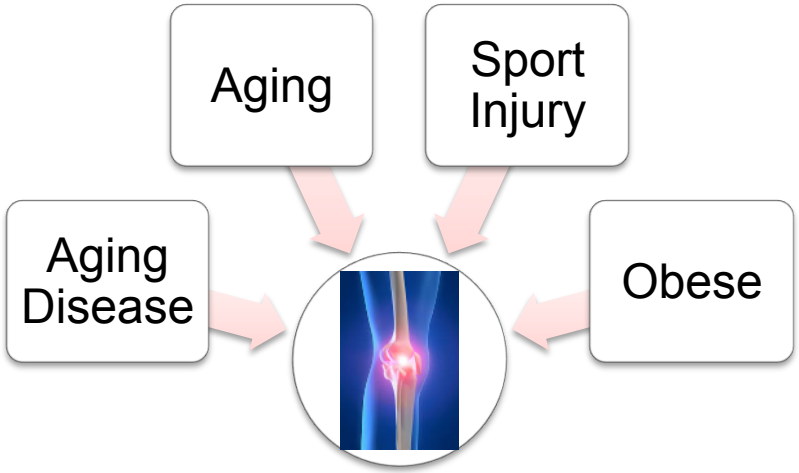
Horizon #2: Knee Replacement Industry Landscape

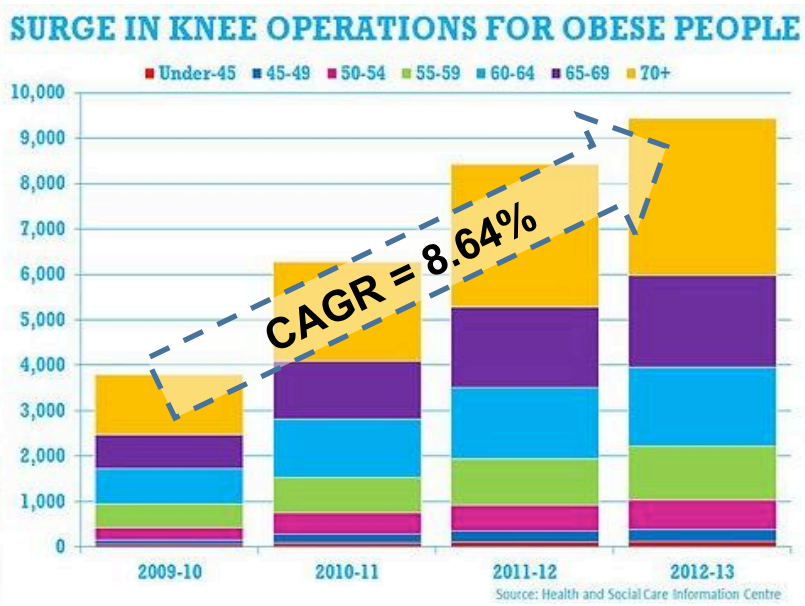


zimmer

stryker
A Global Leader in Medical Technology

DePuy
a Johnson&Johnson company

smith&nephew



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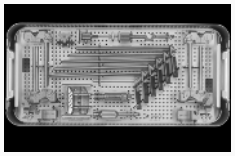
Knee Replacement Technology Comparison

zimmer

Comprehensive Suite

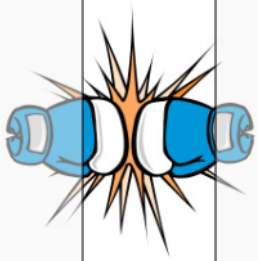
Knee systems (full/partial)

Knee components (tibia, patella)



Knee Instruments

Source: zimmer



CONFORMIS

Image to Implant Technology

2D scan to 3D image

3D Additive Printing

Just-in-Time delivery

Source: conformis

Quality of life!

$3.5K – $4K	**Price***	$6K
12-15 years	**Endurance***	20-25 years
2% serious, 20% unsatisfied	**Patient Satisfaction****	
Limited size and quantity	**Inventory**	On-demand

Source: start-telegram, healthline

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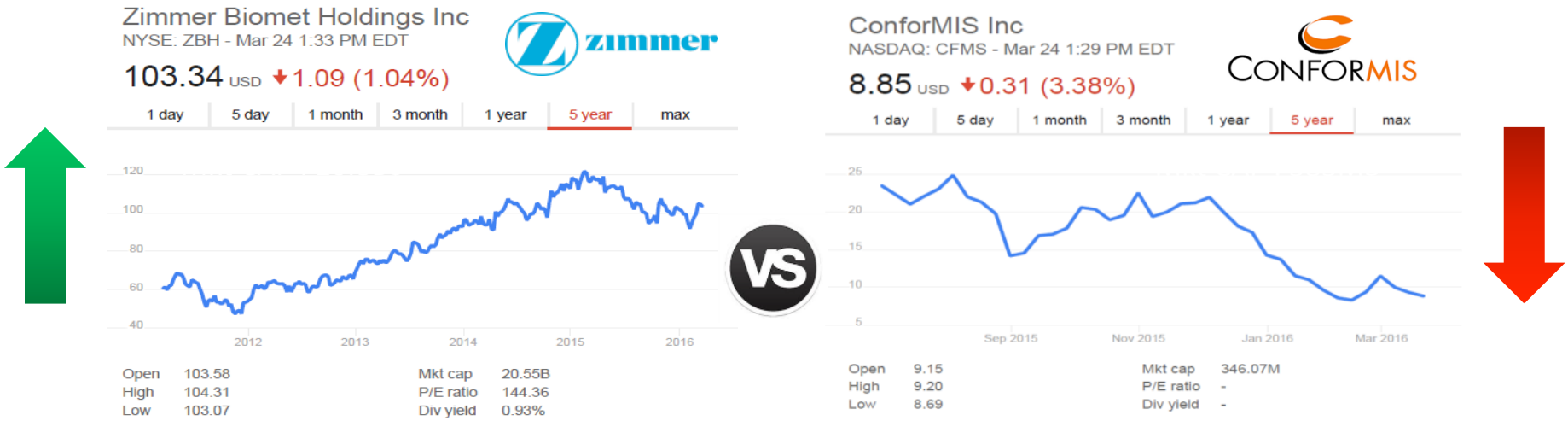
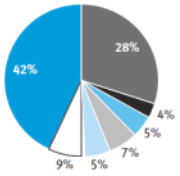
Disconnection of Market Growth

Stock Price Trend



Revenue Trend

Sales by Product Category



	2010	2011	2012	2013	2014	Reported	Constant Currency[1]
Reconstructive	$3,210	$3,355	$3,350	$3,434	$3,496	2%	3%
Knees	1,798	1,836	1,834	1,910	1,966	3%	4%
Hips	1,262	1,356	1,342	1,330	1,326	0%	
Extremities	150	163	174	194	204	5%	
Dental	219	248	238	239	243	1%	
Trauma	246	286	308	316	317	0%	
Spine	234	225	209	202	207	2%	3%
Surgical & Other	311	338	367	432	410	-5%	-3%
Consolidated	$4,220	$4,452	$4,472	$4,623	$4,673	1%	2%

VS

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2015	2014	2015	2014
Revenue				
Product	$ 13,490	$ 12,002	$ 43,953	$ 33,975
Royalty	404	—	3,863	—
Total revenue	13,894	12,002	47,816	33,975
Cost of revenue	10,340	7,351	30,392	21,961
Gross profit	3,554	4,651	17,424	12,014
Operating expenses				
Sales and marketing	10,225	7,083	29,563	22,541
Research and development	3,885	3,969	12,218	11,163
General and administrative	5,656	3,927	16,790	11,775
Total operating expenses	19,766	14,979	58,571	45,479
Loss from operations	(16,212	(10,328	(41,147)	(33,465

Source: SEC.org

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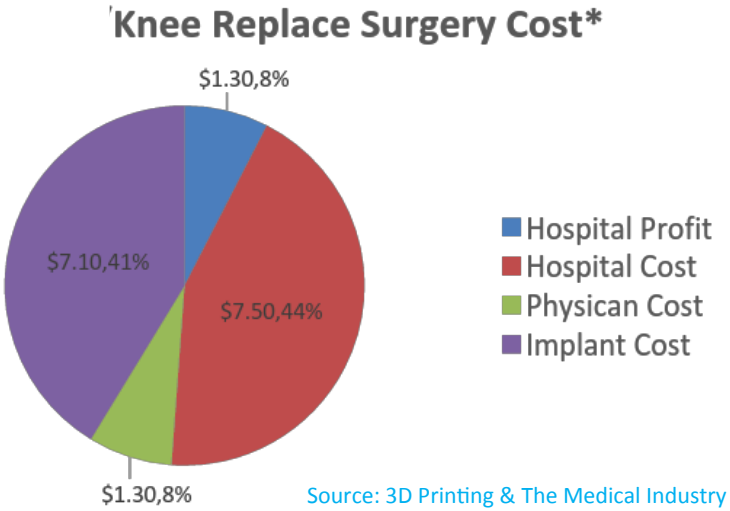
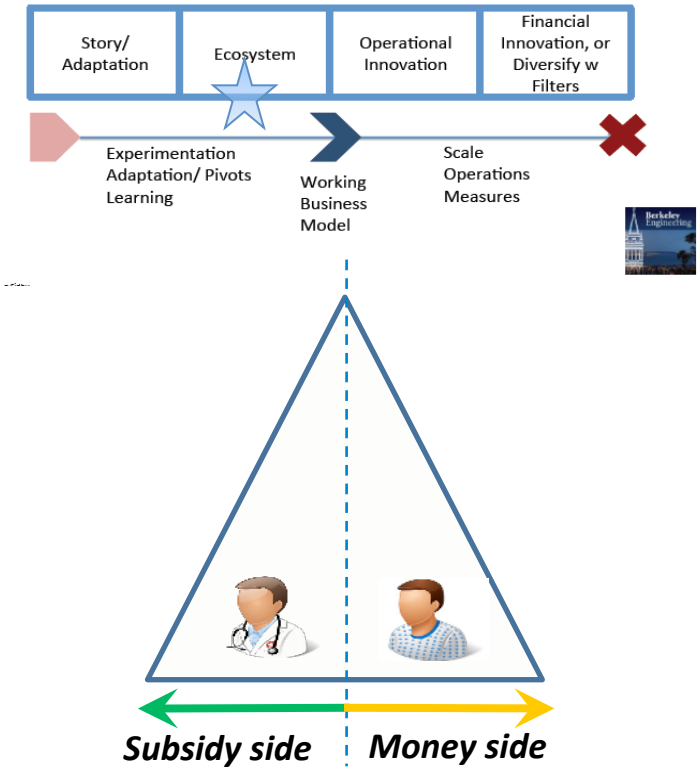
Knee Replacement Eco-system & Subsidy Strategy

Source: Design made by Freepik.com



Source: 3D Printing & The Medical Industry



Physician cost ↓	Lifetime cost ↓
Hospital cost ↓	Life quality ↑

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Horizon #3 : Are We Ready for the Future ?

Scientists hope to one day grow any tissue or organ a person needs

Current waiting list for kidney transplant in US: 93,000 people
Waiting time for a deceased donor: ~5 years (~10 years in some states)

Over 17,000 people approved and waiting for liver transplant.
(source: Inkd.org)

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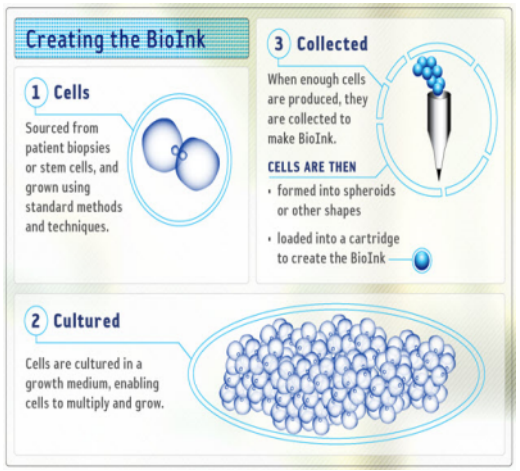
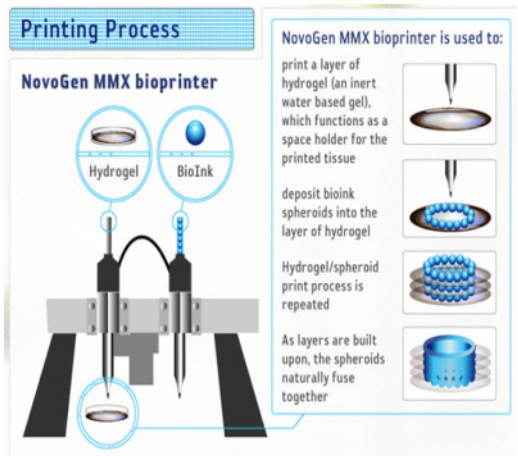
3D Tissue Printing Flow Illustration.

Pre-Processing
Computer Model (CAD, Blueprints), Pre-conditioning

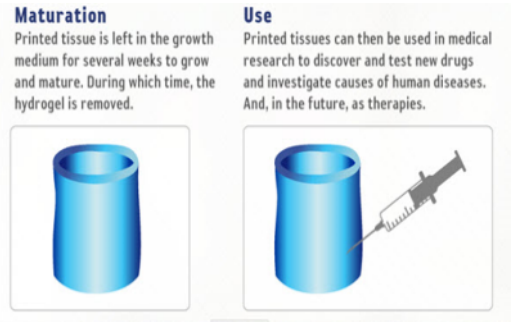


Processing
3D Tissue Printing

Bio-Ink | Bio-Paper | Bio-Printer



Post-Processing
Bio-Reactor, post-conditioning, Tissue Maturation



Star Trek-like technology isn't developed overnight
Organovo has just about the closest thing to it at the moment

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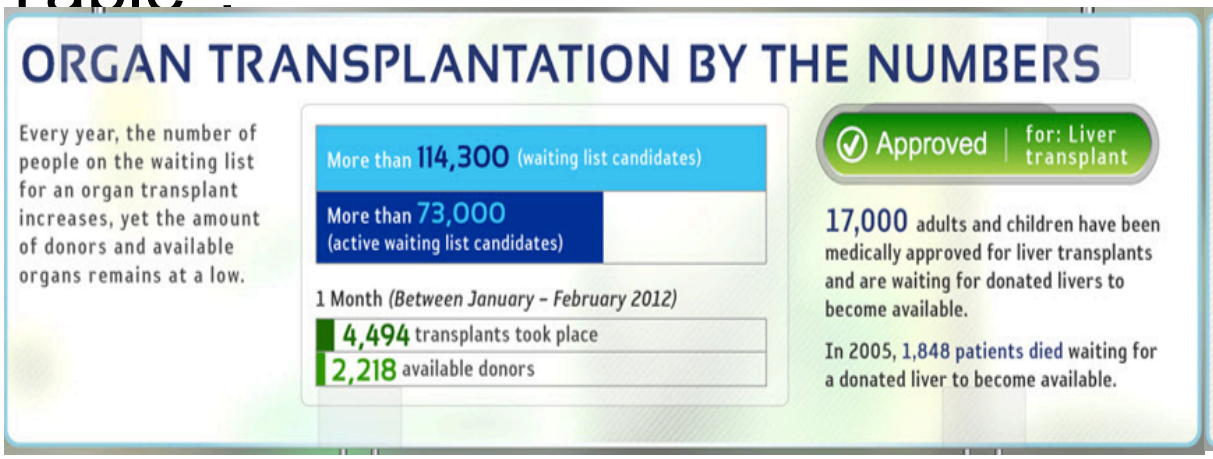
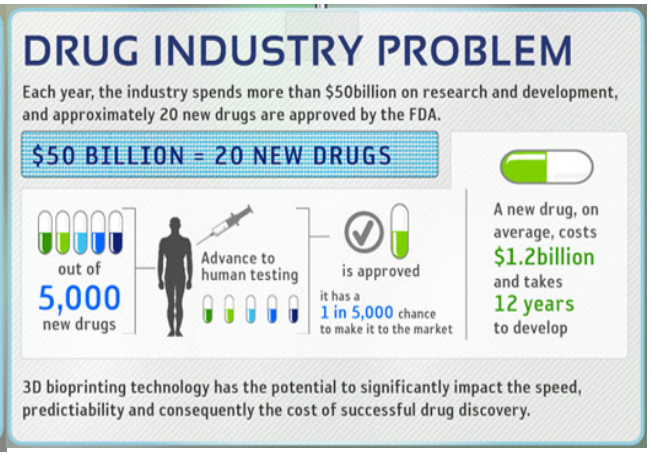
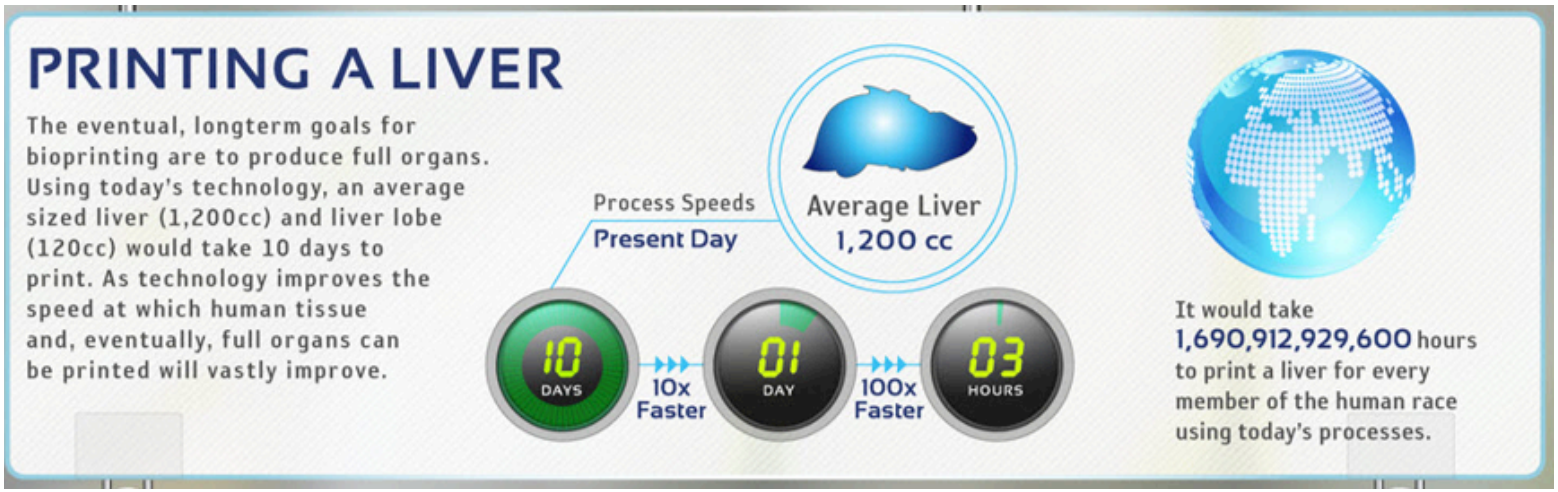
Staging: What can 3D Bio-Printing Bring To The Table ?







printerinks.com

http://www.organovo.com
http://www.unos.org
http://www.liverfoundation.org
http://www.wired.com
http://www.explainingthefuture.com

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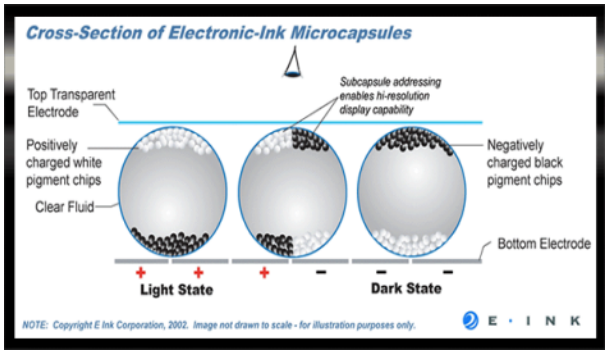
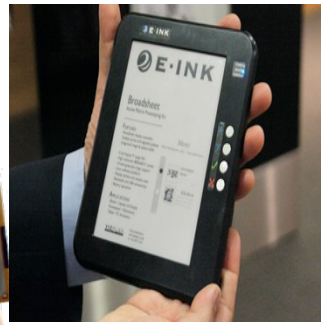
Similarity: E-INK & ORGANAVO

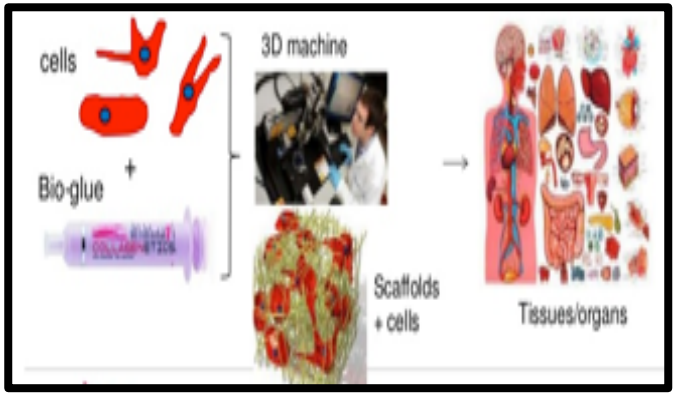
E-INK





GAME-CHANGING TECH

BIO-INK



Similar business challenges: What to focus on? Creating a market, sustainability

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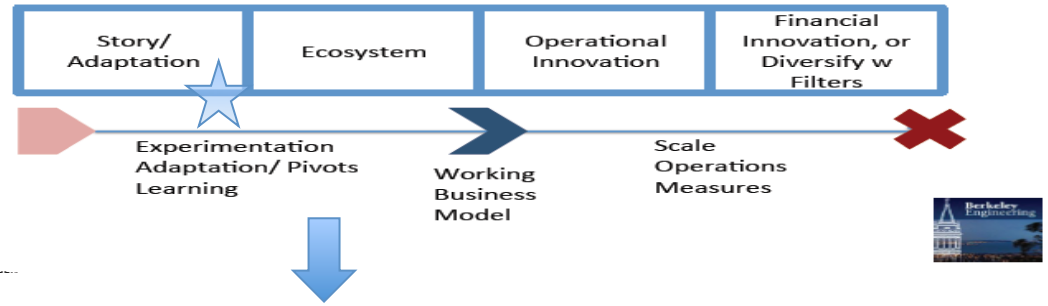
Organovo At A Glance



organovo

CHANGING THE SHAPE OF MEDICAL RESEARCH AND PRACTICE

Core Competency
- 3D Bio-printing technology
- Develops 3D human disease models,
- Accelerating research (better than animal models)
- Platform - novel NovoGen Bioprinter, bio-ink

Product Scope
- Application of 3D tissues - drug discovery / development, biological research, therapeutic implants for treatment of damaged or degenerating tissues and organs
- Revenue Products - 3D Human Liver & Kidney tissues (early stage)

Strengths & Opportunity
- Leader in the space
- Publicly traded
- IP - owns / holds exclusive licenses to multiple patents
- Opportunity – broad applications for unmet needs
- Potential -accelerate drug discovery, enable faster treatment at lower cost

Risk Factors & Challenges
- Not profitable yet
- Business strategy, new and unproven technology
- Regulation & IP risks
- Challenge – Overcome risks, break through either with partnerships or own R&D .

Founded – 2007, Employees 80
Revenue ~0.5M
Cash Flow (-20M)

KEY STATISTICS
Market Cap – $203M

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Organavo: Ecosystem Analysis

Suppliers

SAMSARA sciences

wholly-owned subsidiary, provides high-quality primary human liver cells for a wide variety of in vivo & in vitro research applications

Public

organovo™

exVive3D™ HUMAN TISSUE MODELS & SERVICES FOR RESEARCH

- 3D Human Liver Tissue Testing Services
- exVive3D™ Liver Tissue Performance

3D HUMAN TISSUES FOR MEDICAL RESEARCH & THERAPEUTICS

Research Collaborations

Leverage Bio-* Platform

THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH

NIH National Institutes of Health *Turning Discovery Into Health*

National Eye Institute, NATIONAL INSTITUTES OF HEALTH

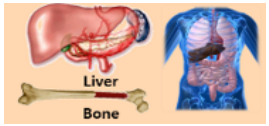
HARVARD MEDICAL SCHOOL

Tissue Therapy,
Complex vascular networks

KNIGHT CANCER INSTITUTE, Oregon Health & Science University

Yale University School of Medicine

METHUSELAH FOUNDATION



Cancer Research

Competition

3D Printing Space

Wake Forest School of Medicine, envisionTEC, TeVido BioDevices, sphero, Hangzhou Dianzi University, HUREL CORPORATION

3D Tissue Space

Modern Meadow, 3Dbots, Aspect, n3D Biosciences, MEDPRIN, 3DISON, 3dbio, TeVido BioDevices, CYFUSE

Competitive Edge – Use of 3D in contrast to 2D

Closely resemble native tissue

Customers

L'ORÉAL

develop 3D printed human skin

MERCK

test medicine toxicity on 3D printed liver cells

Partners

Customize Tissues

Customer focus, ecosystem partnering key for success

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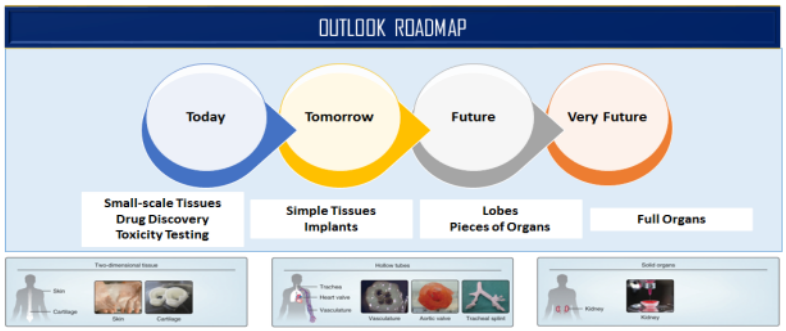
PUTTING IT TOGETHER

3D BIO-PRINTING: Outlook and Opportunities



	2013	2015	2020	2025
Challenges				
Material cost	🔴	🟡	🟢	🟢
Material selection	🔴	🔴	🟡	🟢
Printer cost	🟡	🟡	🟢	🟢
Throughput	🟡	🟡	🟡	🟡
Resolution	🟢	🟢	🟢	🟢
IP/ethical issues	🟡	🔴	🟡	🟡
Adequate design software	🟡	🟡	🟡	🟢
Opportunities				
Local manufacturing and reduced inventory	🔴	🔴	🟡	🟢
Cheaper and more accessible aftermarket parts and repairs	🔴	🟡	🟢	🟢
Novel material compositions and properties	🔴	🔴	🟡	🟡
Multifunctional structures	🔴	🔴	🔴	🟢
Increased premium on commodity materials	🟢	🟢	🟢	🟡
Customization	🔴	🟡	🟡	🟢

Table source: 3D bio-printing: Interview with Anthony Vicari

3D PRINTING MEDICAL : OPPORTUNITY & CHALLENGES

Horizon 1

- **Opportunities –** Expanding international market; parallel markets (iTero scanner)
  Targeted segments (age and treatment groups);
  Treatment enhancements (G4, G5, …)
- **Challenges** – Key patent expirations; deep pocket competition

Horizon 2

- **Opportunities** – Customization, physiologically optimized joint implants
  Comfort and durability, On-Demand (Just-in-Time, lower OPEX)
- **Challenges** – ECOSYSTEM (Dr. / Patient, Insurance), Money / Subsidy side synergy,
  Logistics

Horizon 3

- **Opportunities –** SKY is the LIMIT, Tissues to full functional organs (kidney, heart, liver, ..)
  Organ transplants, Skin/plastic surgery, Faster drug research
- **Challenges** – Approvals, Acceptance, Ethics, Business focus, Sustainability

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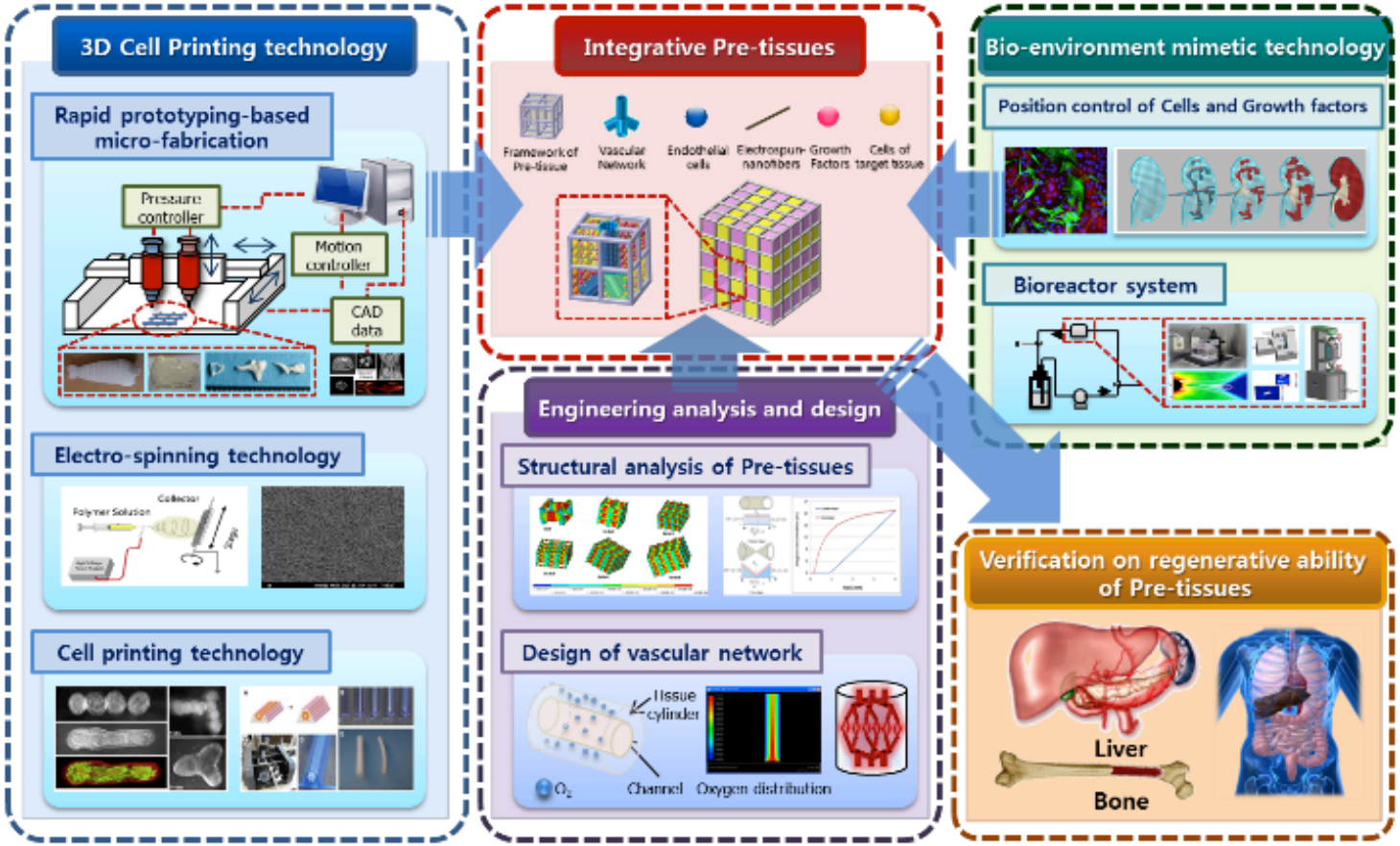
3D PRINTING MEDICAL : Impact Analysis Conclusion

Disruptive Company	Positive Impact (who benefits)	Negative Impact (who suffers)	Impact Timeframe	WHY (and Threats)
Align Technology ***Horizon 1***	Consumers; Orthodontists	Traditional Brace Suppliers	Growing since 1998 FDA approval	**Consumer Satisfaction ; Key IP-protection** **[IP expires in 2017]**
Conformis ***Horizon 2***	Patients, Hospital Inventory	Zimmer – established non-3D MKT leader	< 5yrs	**Ecosystem lagging**
Organovo ***Horizon 3***	Patients cured, War/ accident areas, Organ transplants, Bio-ink makers, CAD software, Drug research	Kidney dialysis ops, Diabetes/insulin ops, Organ logistics/ banks, Pacemakers Stop gap treatments	5- 10 yrs	**Approvals/ Testing, Adoption, Ethics, Cost**

Q & A

COMPLEXITIES IN 3D BIO-ENGINEERING



Source – microfabricator.com article Postech's Intelligent Manufacturing Systems Lab Is Leading the 3D Biofabrication Charge

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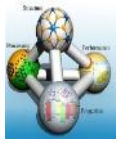
3D BIO-PRINTING: ADOPTION BARRIERS

Material Science Limitations



High Costs (3D Printing & Raw Materials)

Quality Concerns

Acceptance by Health Care Providers, Payers and Patients

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3D Printing – Possible Disruption ?
"Threat or Opportunity"
What should Healthcare Companies Do

Scenario Planning Engagement

Value Capture Assessment

Trigger Experimentation

M&A / Strategic Engagements

Strategy Definition

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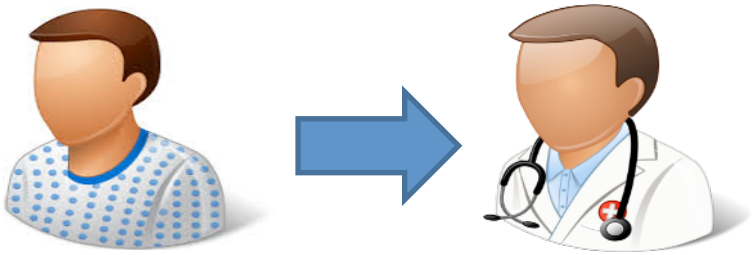
Align: Innovate to Prevent Disruption

- Discuss key patent expiring in 2017
- Introduce iTero as new business segment: adds value to existing product (scanning for molds) and also extends to new products (scanning for implants, bridges, etc…)

	Fiscal Year		
Percentage of Net Revenues by Product	2015	2014	2013
Invisalign Full Products	78%	77%	75%
Invisalign Express Products	11	11	11
Invisalign Non-case*	6	6	7
Scanners and Services	5	6	7
Total net revenues	100%	100%	100%

Conformis : Market Growth & Challenge

- Barrier for Market adoption
  - Within 50miles in BayArea – 5 doctors for conformis 3D knee replacement rather than vs compared to TKR (> 300 doctors).
  - Standford medical center - cemented prosthesis and uncemented prosthesis with TKR.
  - Iowa university medical center for Knee replacement (Top Knee surgeon facility) – Convectional TKR



- Big player will be enter the market for competition.
  - Merged Biomet + Zimmer : Zimmer Biomet announced 3D printed Ankle fusion.
  - Stryker : investment of 3D printing manufacturing facility

Press release: BASK annual meeting for conformis report .(British association of surgery knee)

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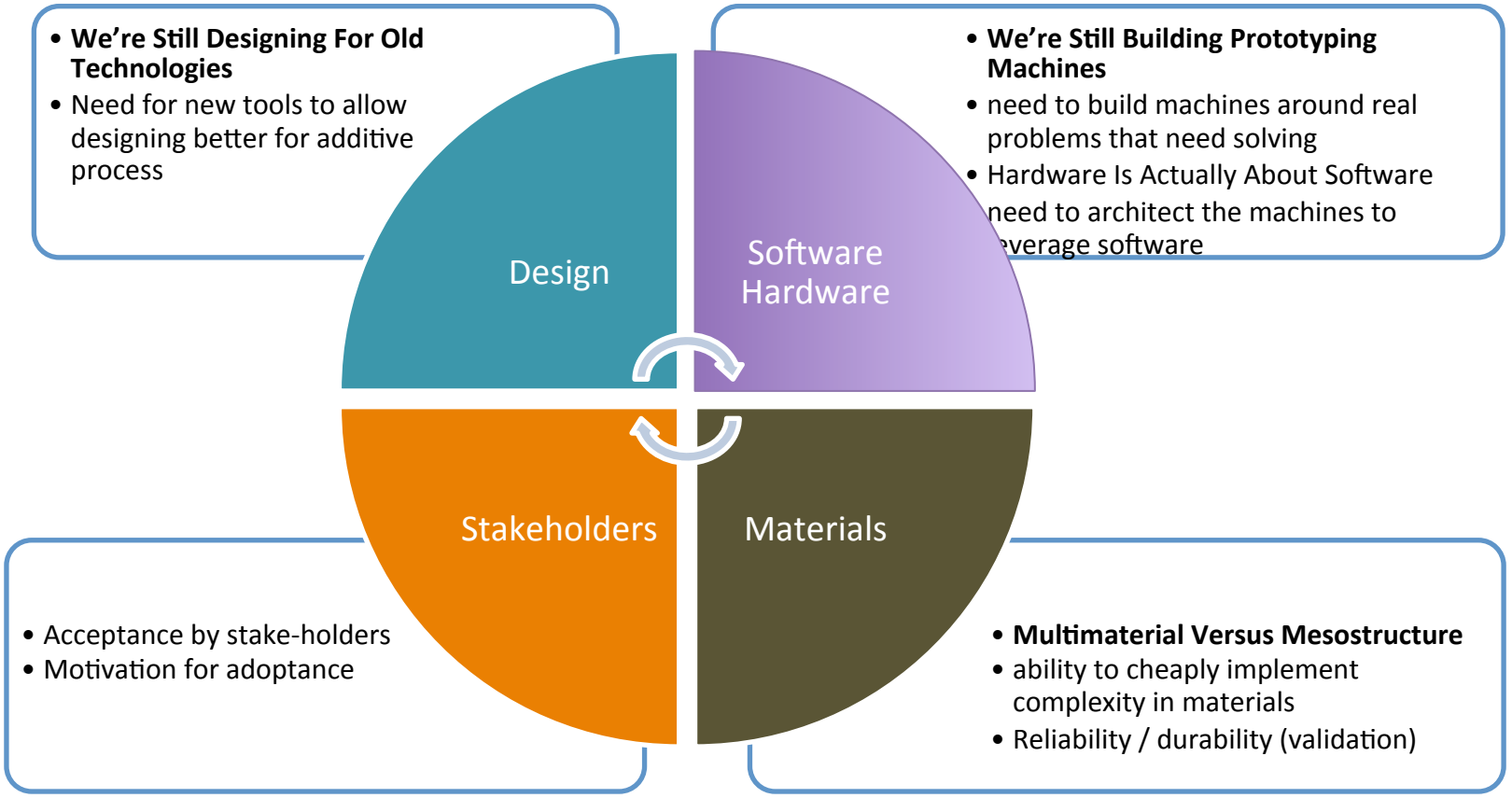
3D Printing Medical Ecosystem Challenges



Old-fashioned ways of thought have prevented us from truly realizing the potential of 3D printing By changing how we think about 3D printing to embrace the systems nature of the family of technologies, we can begin to actually leverage it against real problems.

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