

Sp
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Or
Where Are We in 2015? 15

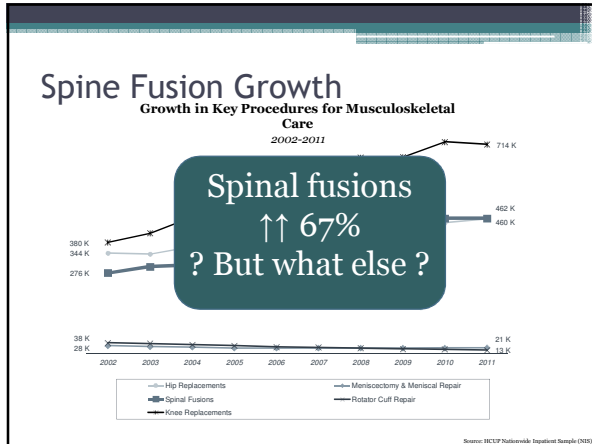
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University of California San Diego

Disclosures

- AO Spine
- Benvenue Medical
- EBI
- Globus Medical
- Intrinsic Therapy
- Johnson & Johnson, DePuy Spine
- Magnifi Group
- Medtronic
- NuVasive, Inc.
- Samumed
- SI Bone, Inc.
- Spinal Kinetics
- Stryker
- Symmetry
- Vertiflex

Acknowledgements

Gunnar Andersson, M.D.,Ph.D.
Robin Young
Cary Hagan
Michael Hubbard





- ## Artificial Discs
- Worked fine (?L5-S1?)
 - Outcomes = Fusion (The goal of the FDA studies) ["no less than"]
 - Complications / Recovery < Fusion
 - Literature / RCTs → support use

- Lumbar TDR 700+ articles/abstracts
- Cervical TDR 300+ articles/abstracts

Almost all Good - Excellent
Many RCTs

Lumbar

- FDA approves
- NASS fights against its' use
- Insurance will not pay
- Not used

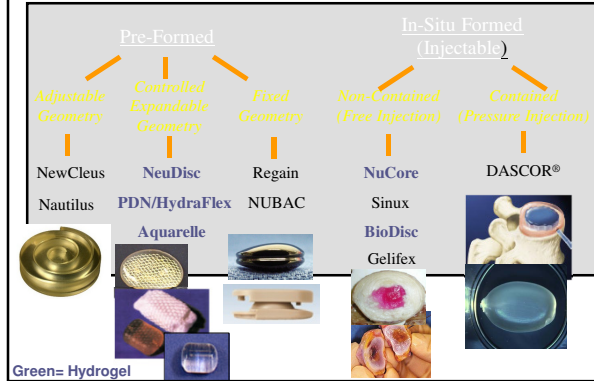
Cervical

- FDA approves (a few companies)
(Companies sue each other)
- NASS fights against its' use
- Only a few insurances pay
- Limited use

Nucleus Replacement



Nucleus Replacement Options



Mechanical

- PDN – Raymedica **Off Market**
- Neodisc – Nuvasive **Off Market (no sales)**
- Neudisc –
Replication Medical **Didn't get past trials**
- Regan – EBI **Off Market**
- Nubac – Pioneer **On the shelf**

Injectables

- Injectable Hydrogel
(Nucore) Off Market

- Biocompatible Polyurethanes
& Containment Balloon
(Dascor) Company Closed

Annular Repair

- Mechanical
- Biologic
 - Primary
 - Sealant
 - Ingrowth

- Biologics
Off market

- Mechanical
Long, slow trials
New companies trying



- Some approved
- But poor / limited use
- Many explanted, or failed
- Many companies closed

Flexible "Rods"
(Approved as Fusion Devices)
(LOL) ↓↓ (☺)
FDA: Extended market surveillance to see if fusing

Facet Arthroplasty

Almost all off market or Company closed

Applied Spine Stabilimax NZ

DePuy

Globus AccuFlex

Scient X Isobar-TTL

Archus TFAS

Medtronic Agile

What is new Now?

Spine Technology Awards 2014 (R. Young)

Cervical Care

Year	Number of Submissions
2009	12
2010	6
2011	4
2012	5
2013	4

Motion Preservation

Year	Number of Submissions
2009	15
2010	4
2011	2
2012	2
2013	2

Minimally Invasive Care

Year	Number of Submissions
2009	19
2010	10
2011	13
2012	15
2013	18

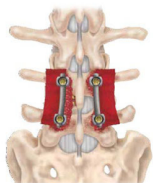
Cervical Care (Second Chart)

Year	Number of Submissions
2009	15
2010	8
2011	3
2012	3
2013	3



Top Ten New Spine Technologies 2014

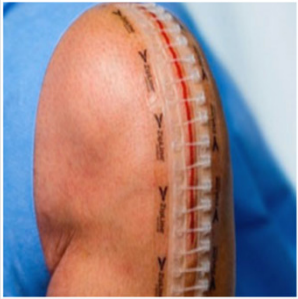
R. Young



MAGNIFUSE II

Demineralized allograft bone with recovered autograft packed into a unique, self-contained, resorbable mesh bag using the provided disposable funnel and plunger. The surgeon can then place the fully contained construct into bone voids.

Medtronic Spine




Skin Closure provides a non-invasive alternative to staples, sutures and glue for surgery and lacerations.

ZipLine Medical Inc.

Lesray is an **image enhancement platform** designed to take low quality, low radiation images and improve them to look like conventional full dose images.



SafeRay Spine, LLC



Scolioscreen

A medical device to be used in combination with a **smartphone** for the early detection of spinal deformities such as scoliosis.

Spinologics, Inc



G-Arm Multi-Plane Surgical Imaging

Whale Imaging

Provides bi-plane views and allows both AP/LT anatomy to be viewed live and simultaneously at up to 25fps on each plane.



109 Design

"smart" strap that replaces the existing straps of a scoliosis back brace. These straps can measure how long and how tightly the braces are being worn and then sends the real-time data to a smartphone application using Bluetooth Low Energy.

Smart Strap

Aesculap, Inc

Direct visualization through an endoscope.
No radiation.




S4 Element MIS



MySpine Patient Matched Technology

Low dose patient CT scans and unique 3D planning tools to create patient-specific anatomical drill/screw placement guides to simplify pedicle screw placement during spine surgery.

Medacta International SA




NLT SPINE

It is comprised of two sub-sets: the single-use ARC percutaneous pedicle screw, consisting of a full array of lengths and diameters, and a set of reusable instruments

ARC Pedicle Screw System

SafeWire, LLC



Pedicle Access Needle with Broach is designed to improve the surgeon's workflow, depth accuracy, and reduce the need for fluoroscopy when accessing the pedicle

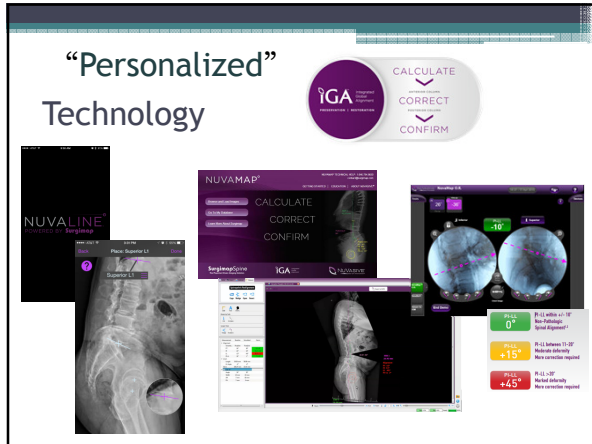
Tiger Express



Vital 5, LLC

Dual function directional analgesic infusion catheter and wound drainage system.

ReLeaf Anesthetic Delivery Catheter



NO Game Changers Here

Just “Add-Ons”

(Except for Diagnostics and maybe “Personalized” / Automated Implant Technologies)

Conclusion

- Regulations are killing major innovation at a time when it is needed most...
- Development should focus on “unmet clinical needs” without being bound by reimbursement considerations...
- Major advancements are not occurring because of the tough conditions which results in only small steps forward...

Small Companies Deliver Innovation

- U.S. Start-Ups are Innovation Engines
 - 93% of medical device manufacturers have < 100 employees
 - Collaboration of researchers, physicians and corporations

U.S. Medical Device Manufacturing Companies by Number of Employees

Employee Count	Percentage
>500	2%
100-499	5%
20-99	14%
10-19	10%
<10	69%

Source: FDA, CDRH

C. Hagen

Innovation Dilemma... Investors Avoid:

- PMA projects
- Projects requiring new reimbursement codes

C. Hagen

Small Companies (Spine) Nearing Extinction

- Investment in Devices down by 42%*
- Investment in Ortho-Spine has been reduced by 58%

(\$1.49B in 2006 to \$479M 2013; Source: WSI Sept 15, 2014)

VENTURE INVESTMENT MEDICAL DEVICES AND EQUIPMENT

Year	Investment (\$M)
2007	~\$30M
2008	~\$30M
2009	~\$22M
2010	~\$20M
2011	~\$25M
2012	~\$22M
2013	~\$18M

PricewaterhouseCoopers / National Venture Capital Association
MoneyTree™ Report, Data: Thomson Reuters
Total U.S. Investments by Year Q1 1995 - Q2 2014

C. Hagen

Result: Incrementalism

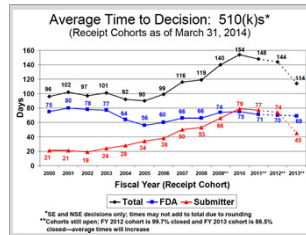
- Only small improvements to existing technologies are possible (510K)
 - US regulatory & reimbursement challenges have nearly eliminated available capital from investors due to:
 - Regulatory costs/uncertainty
 - Forced clinical trials overseas
 - Delayed reimbursement
 - ?? Reimbursement ??
 - Insurance
 - NASS

Tough Regulatory Environment

Highly uncertain process stifling innovation

- Improving, but lengthy, approval timelines

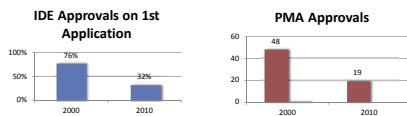
*2/3 of small MD&D companies receive EU clearance first**



* Source: Northwestern Univ. survey of 356 med device manufacturing reps and regulatory affairs professionals

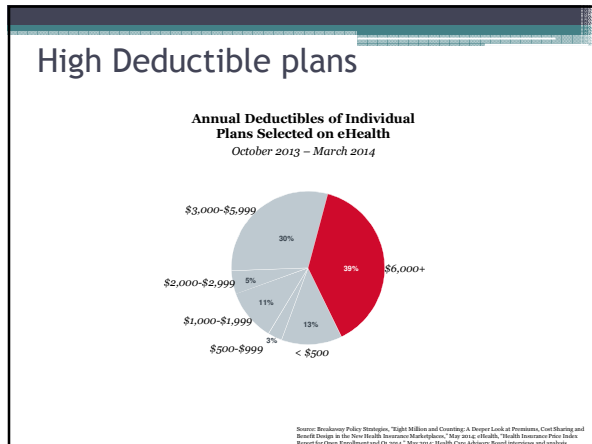
Metrics: FDA Rejections

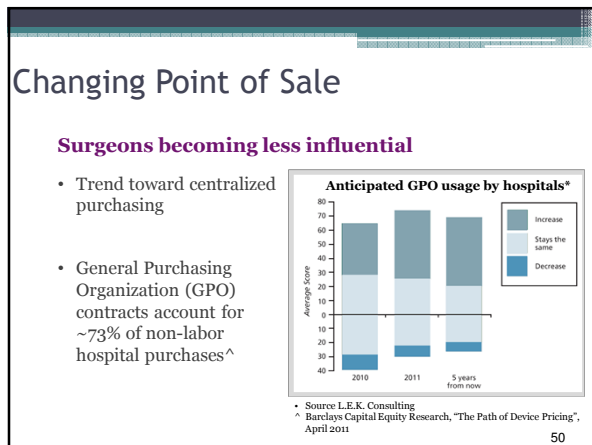
- Reduction in IDE studies and PMA approvals

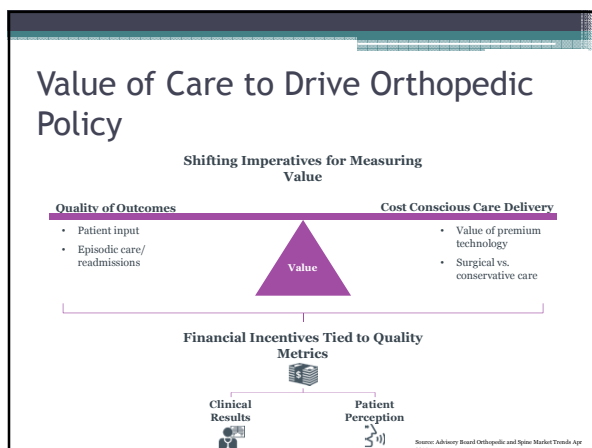


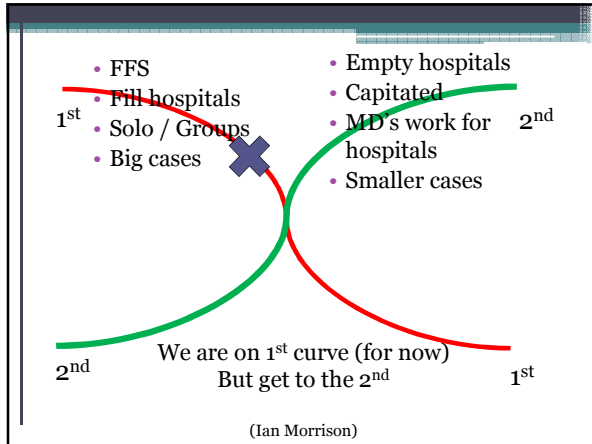
Source: Makover, et al., November 2010, FDA Impact on Medical Innovation

- 40% decrease in IDE Approvals
- 60% decrease in PMA Approvals



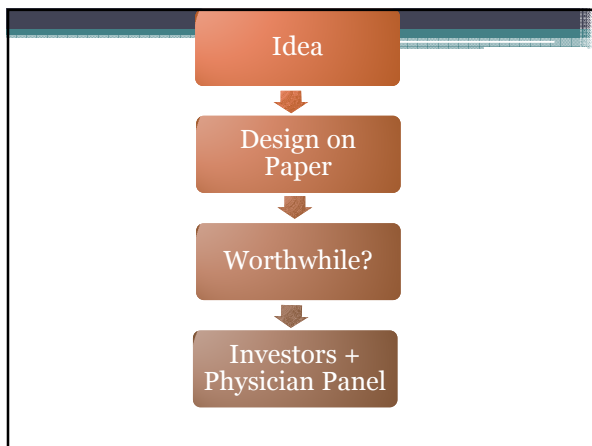




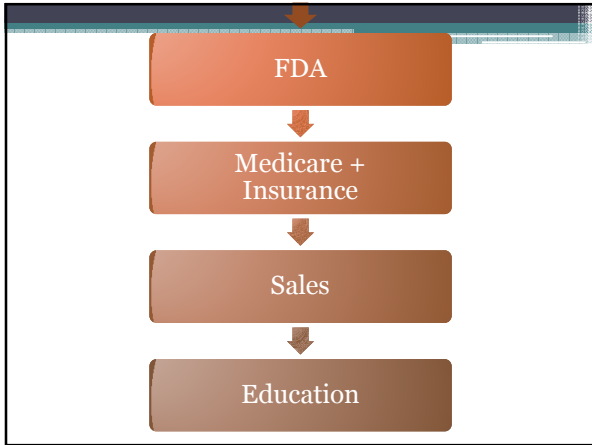


NEW TECHNOLOGY DEVELOPMENT

DECISIONS/INFORMATION	INDUSTRY	PROFESSION
What is needed?	??	xx
What technology is available or coming?	xx	??
Patients to assess/access	0	xx
Protocol (study/development)	x	xx
Money for clinical (or basic) research	xxxx	
Presentations (papers)		xx
Education	xx	xx
Marketing	xx	+/-









S.A.B.

want rewards

- Involvement in study
 - Presentations
 - Publications
 - Prestige
- Patient care improvement
- Solve a clinical problem
- Consulting time fees
- Stock options



Presentations/Publications

DISCLOSURES

Is that enough?

Is it valid?

Is what you hear/read the real truth?

CLINICAL RESEARCHER

If (+): want rewards (early phase)

Developers/SAB: want academic recognition

BUT

Clinical studies should be by others not rewarded financially

Who will do that work?

INDUSTRY

Aware of conflicts
Sales
Stay "clean"
But promote
Sell
Get studies done and published

Publication/Presentation

Disclose Financial Associations

↓

Taints Study

Why?

Who else would do early?

Who else cares early?


But

If not invited into trials early

Mad

Angry

Denigrate studies



N.I.H. Funding

Publications any cleaner?
Any less "tainted"?
(Need to publish something)

N.I.H.

Easily accepted
No boxes to check
"Pure"

But is it?

How do you get refunding?
Negative results?
or
Positive results?

Do you return the money if negative?
Put a positive "spin" on the results?
Publish negative Results?

**INDUSTRY FUNDED STUDIES
REPORT POSITIVE RESULTS MORE
OFTEN THAN NON-INDUSTRY**

Non-industry studies

50% neutral results

Industry funds

only 20% neutral results

Shah, Alberts, Vaccaro
Spine 2005

However

Early clinical trials in limited patients too few with too short follow-up for publication

This leads industry and M.D. to pursue larger enrollments – with positive results anticipated (and known from trials)

So should be positive

If early results negative, the project would be dropped

And

If results of clinical trial poor and project (implant-drug) dropped –

Why publish it?
Who would care?

Maybe these are the reasons studies are mostly positive

But

Any publication for N.I.H. (or non-industry funding)

Is worthwhile -

for personal CV

So neutral (often non-helpful) findings are OK

Is the relationship "tainted"?

Is it over blown?

Are only those uninvolved pure?

AAOS News

- Physicians who become involved in the business side of medicine – as inventors, educators, or consultants – must do so carefully and ethically, placing their responsibility as healthcare providers over financial gain.

Total Biomedical Research Funding (U.S.)

1994	\$37 billion
2003	\$94.3 billion

57% Industry (↑over time)
28% N.I.H. (↓↓↓ over time)

Medical Product Co.

- 58% total US research funding
- 70-80% worldwide from US companies

But
Real \$\$ going down

ortho.com
2011

Funding

	NIH/NIAMS	→	For Orthopaedics
2004	\$499,417,000 Priority Score 154		\$126,680,000
2005	\$507,755,000 Priority Score 150		\$114,000,000
2007	\$507,292,000 Priority Score 144		\$50,247,620 (\$36,255,716)
Now	↓↓↓		↓↓↓

(NIAMS: Arthritis/Bone-Muscle/Skin)

NIH Funding

- ↓ 2% in 2008
- ↓ 8.6% 2003 → 2007 (inflation adjusted)

JAMA Jan 13, 2012

NIH

Decreasing funding
Increasingly rigorous and difficult

Industry

Decreasing innovative product funding
↓ ↓
Increasing scrutiny

R&D Spending

2013 <ul style="list-style-type: none">• Annual Sales: 1.6 billion• \$ for R&D: \$98 mil• R&D as % of Sales: 6%	2014 <ul style="list-style-type: none">• Annual Sales: \$1.9 billion• \$ for R&D: \$129 mil• R&D as % of Sales: 7%
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But what is in R&D?

FDA

"Beat the Gold Standard"

"No worse than" no longer works

Proven medico-economic benefit

But have to do the studies to decide

- Very long
- Very expensive
- Very challenging

Future Treatment

Biology > > implants

Long term studies

How long follow for biologic consequences?

\$ Who funds \$

And Now This
 e.g.: Challenges:
 Standard device trying to get into existing FDA cleared and Medicare coded market
 Trial protocol updated by FDA
 Local, won't
 app
 Biologic: Small
 degenerative pro ects
 Phase 1: FDA requirements
 Females: None with child bearing potential;
 Males: must abstain or wear protection for 12 months

Could you predict this???

RCT's 2 year follow-up for publication/FDA
 Who supports?
 Who follows?
 Who collects data?
 Who reports?
 Multi-center co-ordination?

How "clean" is enrollment in surgical trials?

Who Funds?

- Private M.D.
- Universities
- Developer/VC
- Medical Societies
- Industry

Going overseas cheaper, easier, quicker

The
Company-Physician
Partnership

From the legal perspective

The relationship between
industry and physician is
critically important.

Companies cannot develop and
introduce new and useful
technologies in a vacuum -- need
practical input from physicians.

Physicians' inability to interact fully with companies will delay, potentially indefinitely, the introduction or improvement of technologies.

The relationship between industry and physicians is increasingly scrutinized

Subpoenas to orthopaedic and cardiac companies, investigating potential violations of U.S. anti-kickback laws based on company-physician relationships

Adoption of restrictive codes and policies by governing organizations

Prosecutions of Drug companies

Eroding public trust in the medical industry due to recent

- malfunctioning products (pacemaker recalls)
- malfunctioning drugs (Vioxx)
- corporate scandals

US government has subpoenaed records from every orthopaedic company to determine if

Any company has broken the law in collaborating with surgeons by providing "money" – (not appropriate compensation)

**Biomet, DePuy,
Smith & Nephew, Zimmer**

- 2002-2006
 - \$800 million on 6,500 consulting agreements

- 2007
 - Settled with US Government
 - \$310 million + Government supervision

- (also Stryker and Wright)

Relationship Restrictions

- Laws (e.g., Anti-Kickback, False Claims)
- Professional Society Codes of Conduct (AdvaMed, AMA)
- Internal company codes and policies
- Hospital codes and policies (OIG guidelines)
- Contractual provisions between Industry/M.D.
- Sunshine ACT (\$10)

CONSIDERATIONS

The stronger the relationship between company and M.D., whether through

prominence (senior advisor, technical, advisory board)

volume of business from M.D.

total consulting fees paid

the more likely the relationship will be subjected to scrutiny.

CONSIDERATIONS

If business is conducted, it must be documented

Companies cannot afford to risk their futures based on questionable demands of a few physician consultants

Physicians cannot afford to work with companies that overlook the existing restrictions
(and vice versa)

Ethical responsibility to set an example by all actions

US Surgeon Brand Loyalty Varies Widely between Specialties
 Details of How Differing Specialties Make Medical Device Purchase Decisions Quantified by Millennium Research Group's New

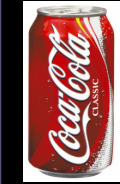
“Spine surgeons & neurosurgeons, plastic surgeons, and orthopedic surgeons tend to be more loyal to a single medical device company and purchase most of their products from just one or two manufacturers.”

Other specialties are much more likely to switch brands or purchase from multiple medical device companies simultaneously.


60 more loyal to a single medical device company and purchase most of their products from just one or two manufacturers. Other specialties are much more likely to switch brands or purchase from multiple medical device companies simultaneously. MRG's latest Perception Pulse illuminates this and many other differences.

THE OBVIOUS NEGATIVES?

Research presentations biased toward company product
(consultation fees, research/clinical support)



**“Favorites”
cannot be
avoided.**



- The Institute of Medicine (IOM) of the National Academies' Committee on Conflict of Interest in Medical Research, Education and Practice has held at least three open hearings regarding industry relationships

- "This conflict of interest examination investigation looks broadly at medical research, education, as well as private practitioners, and the potential conflict of interest"

David Lovett, J.D.; AAOS

- We believe that a collaborative relationship is necessary to improve patient care, but we also recognize that it must be carefully scrutinized to avoid pitfalls of improper endorsements either real or perceived."

David Rawling, M.D.; AAOS

Conclusion
Not much change (2015)
Nothing exciting (game changing)
In near horizon

Financial Changes }
Business Changes } For Spine Surgeons in 2015



Thank You