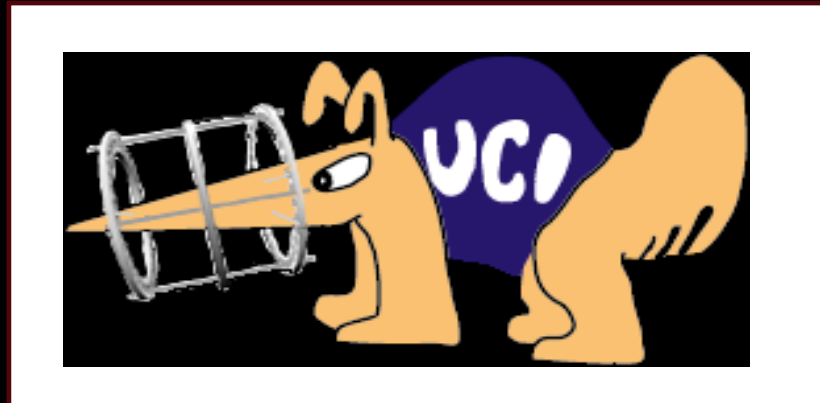


The Evolution of Medical Technology: The Historical Perspective

STUART A. GREEN, MD
UNIVERSITY OF CALIFORNIA, IRVINE



- Orthopaedic Surgeons: Inheritors of Tradition
Green SA, Clin. Orthop. 363:258-263, 1999
- The Evolution of Medical Technology
Green SA, Clin. Orthop. 385:260-266, 2001
- The Origins of Modern Clinical Research
Green SA, Clin. Orthop. 405:311-319, 2002
- Surgeons and Shamans:
The Placebo Value of Ritual
Green SA, Clin. Orthop. 450:249-256, 2006



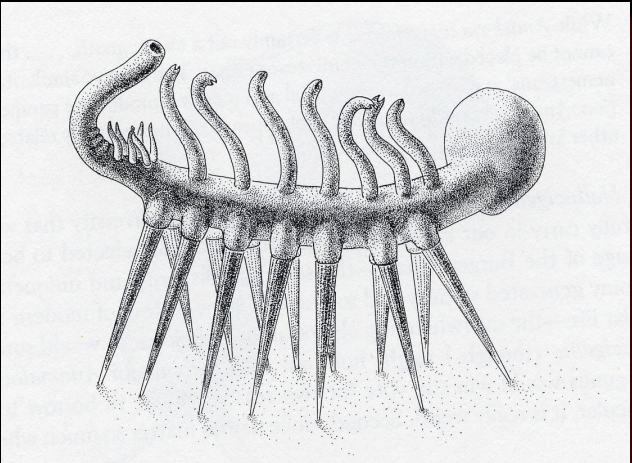
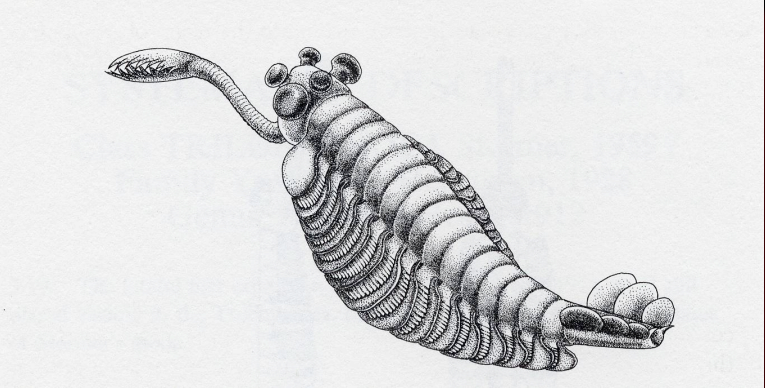
Dear Doctor Franklin
*E-mails to a Founding Father about
Science, Medicine, and Technology*

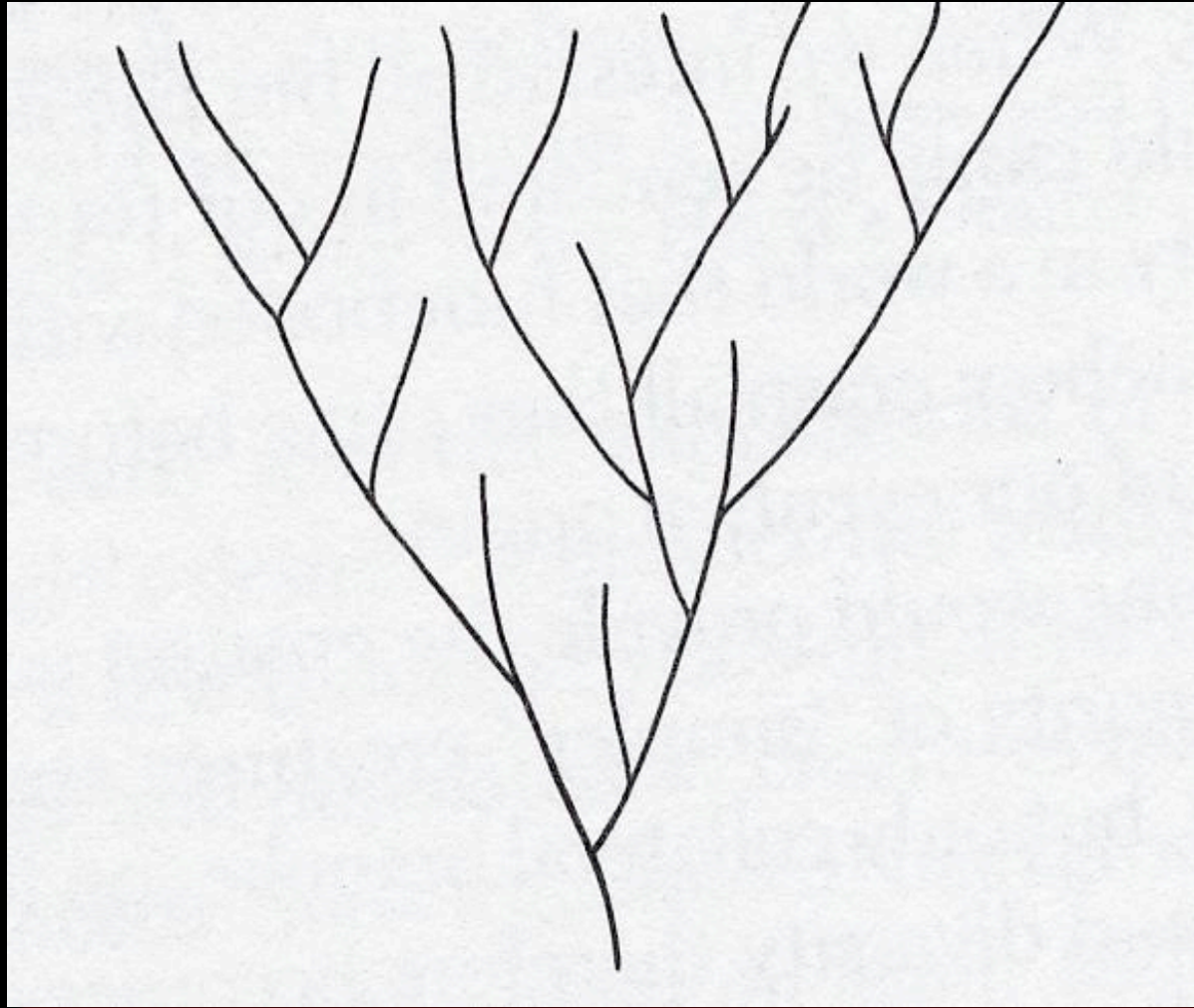
Stuart A. Green, M.D.

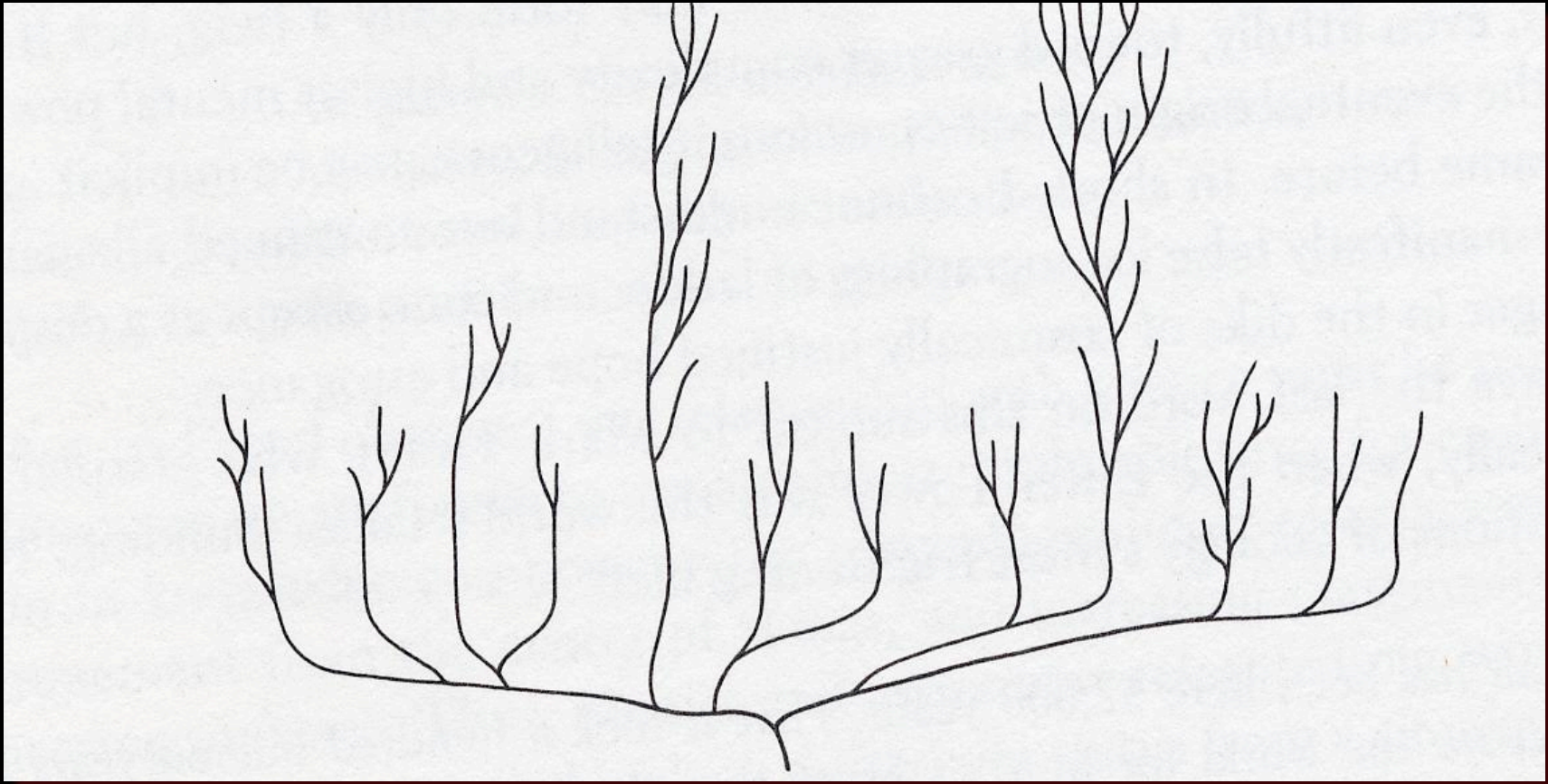
The Evolution of Medical Technology: Lessons from the Burgess Shale

Clin. Orthop. 385:260-6, 2001









DIVERSIFICATION & DECIMATION

A feature of all “empty landscape”
biologic systems

S.J.Gould

DIVERSIFICATION & DECIMATION

**A feature of all complex systems
evolving in an empty landscape
environment**

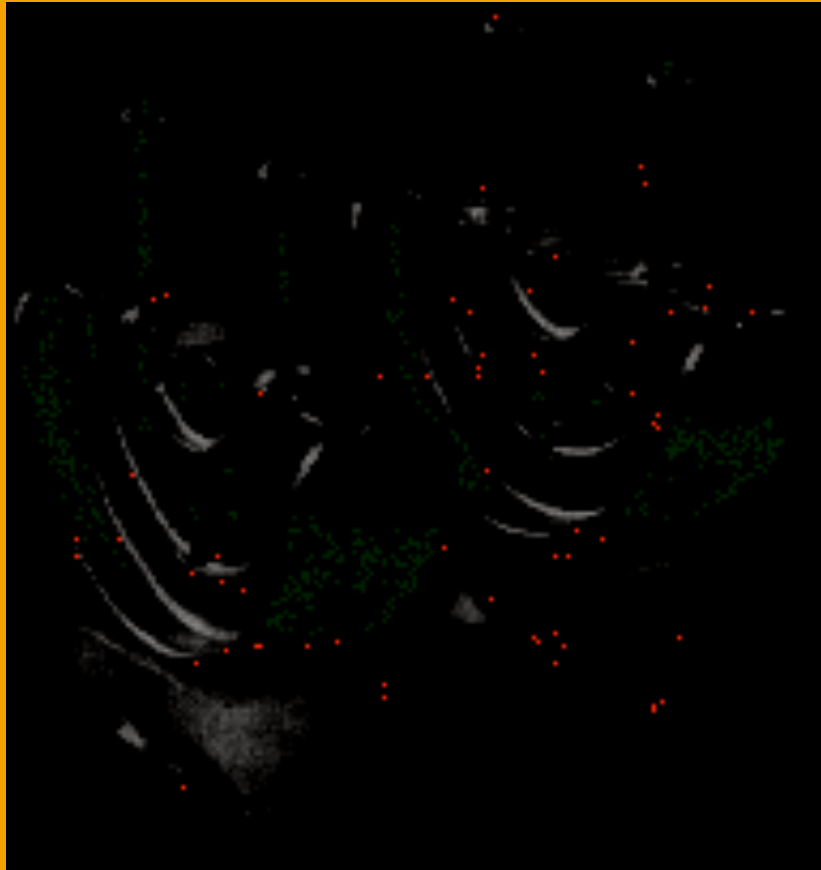
S. Kauffman

DIVERSIFICATION & DECIMATION

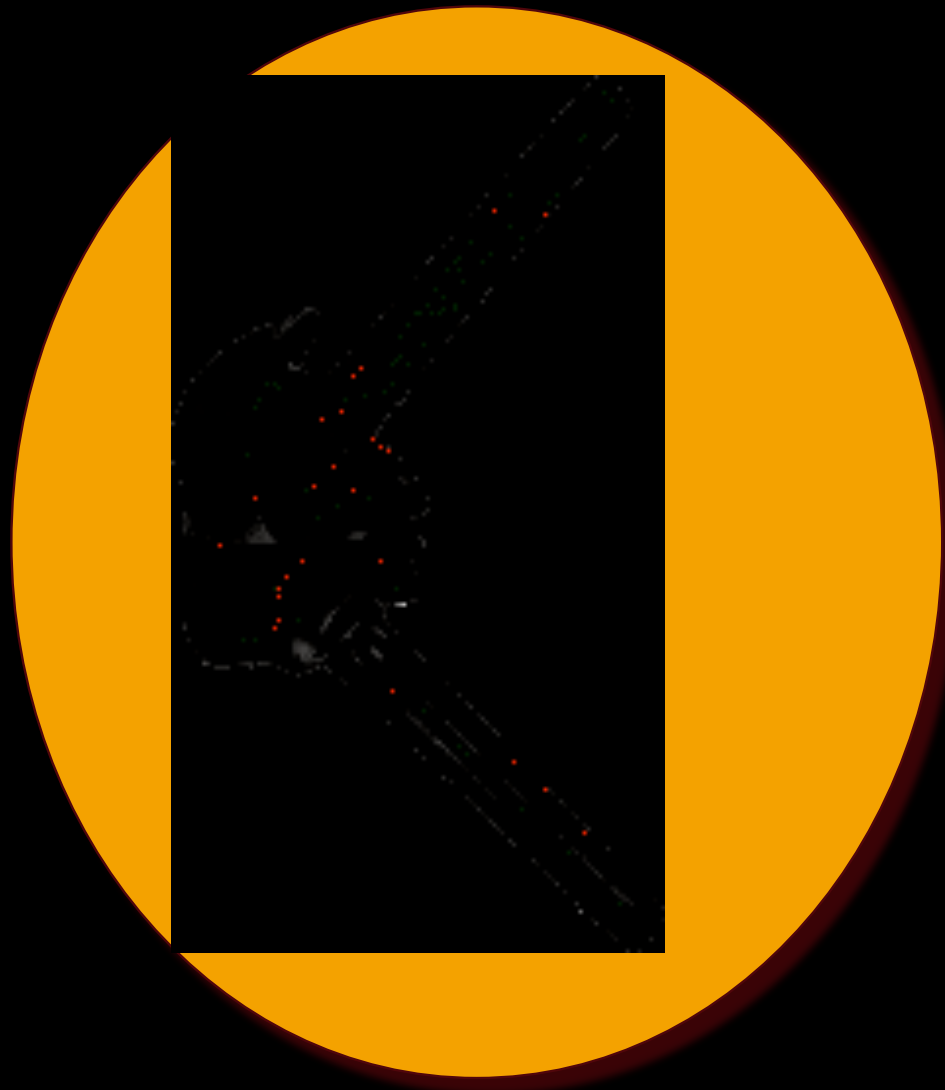
- **automobile**
- **computer operating systems**

DIVERSIFICATION & DECIMATION

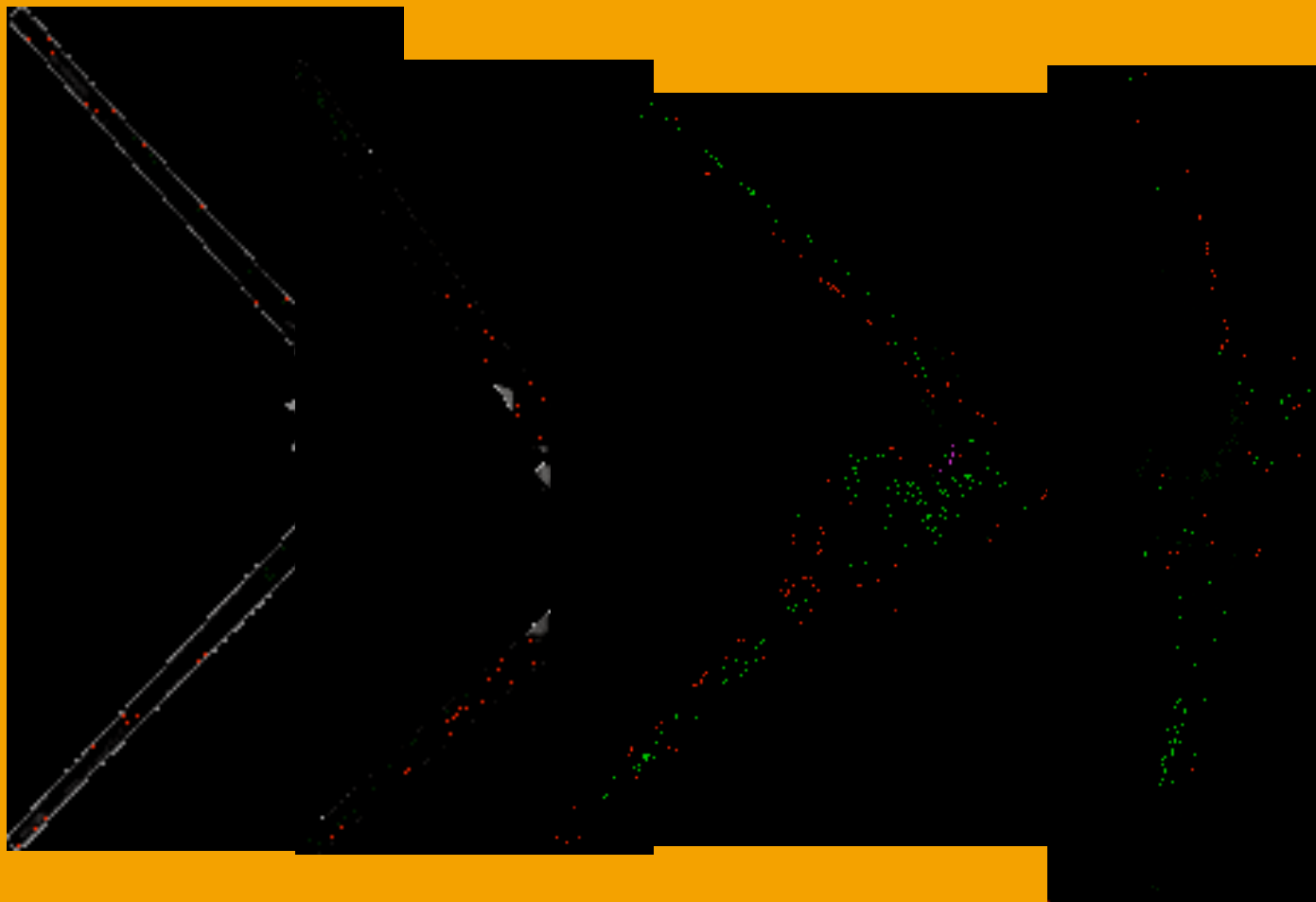
Total Knee Replacement



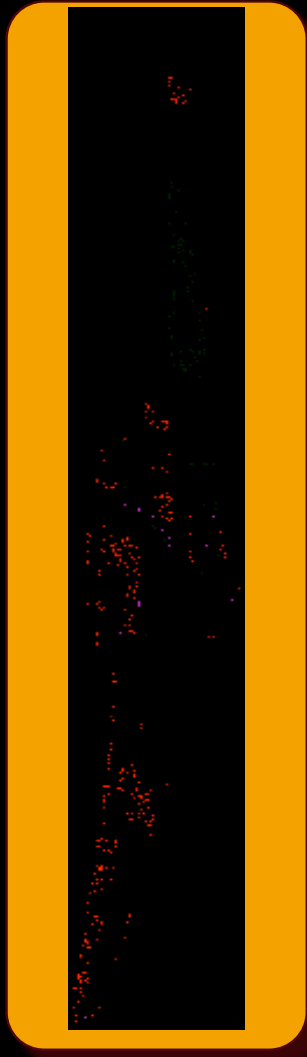
GUNSTON



WALLDIUS



YOUNG SHIERS SHEEHAN GUEPAR



HERBERT



ELSON-WATTS



MADREPORIC



LL



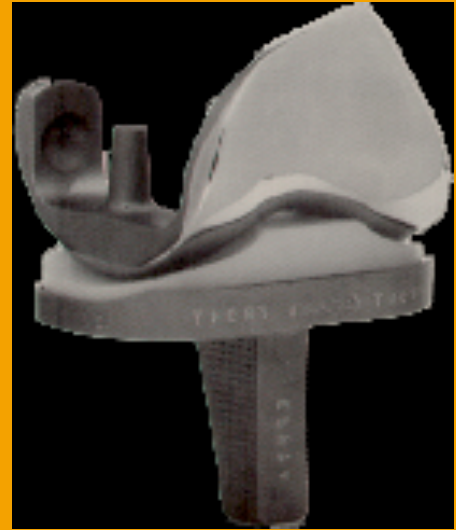
ST. GEORGE

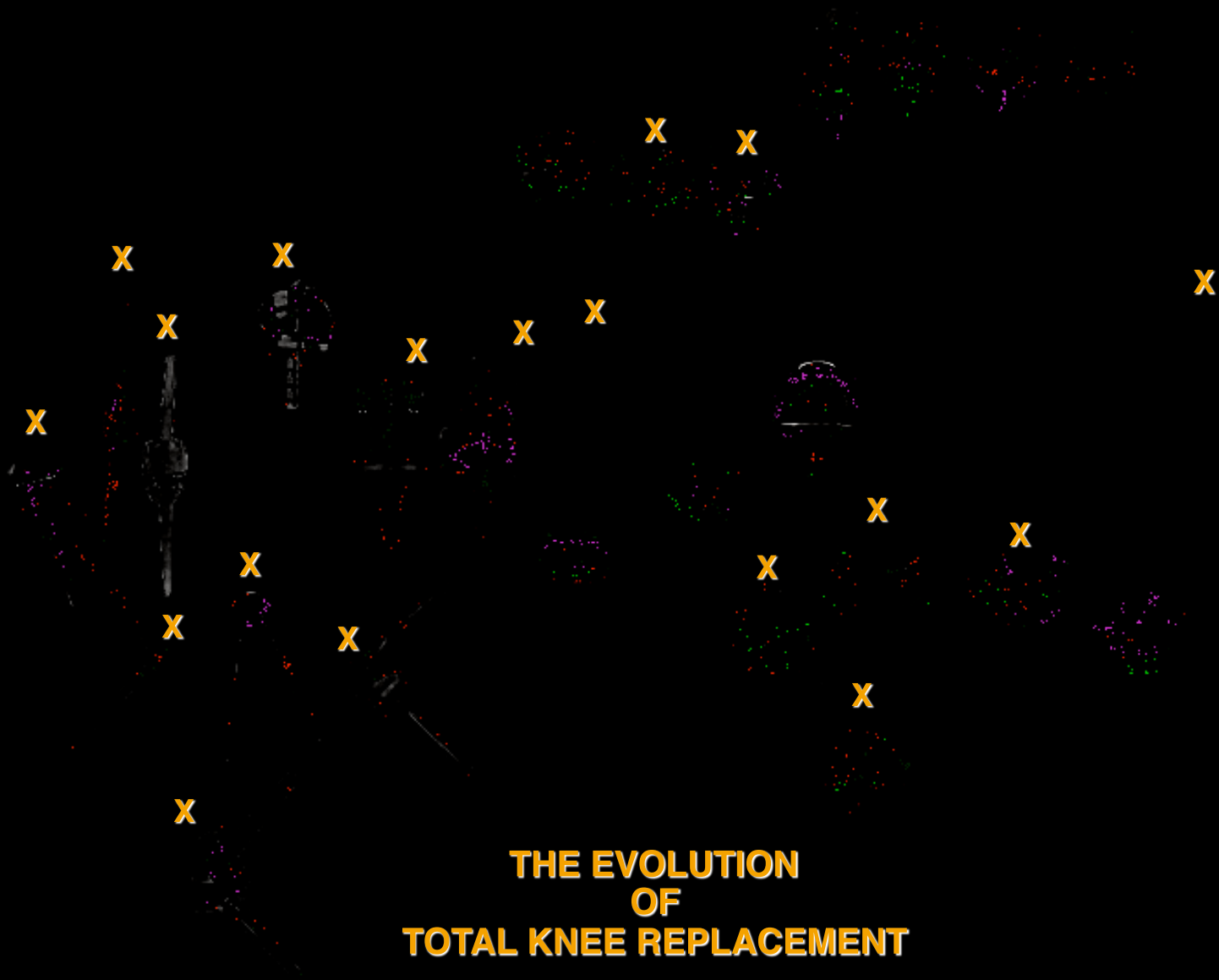


UCI

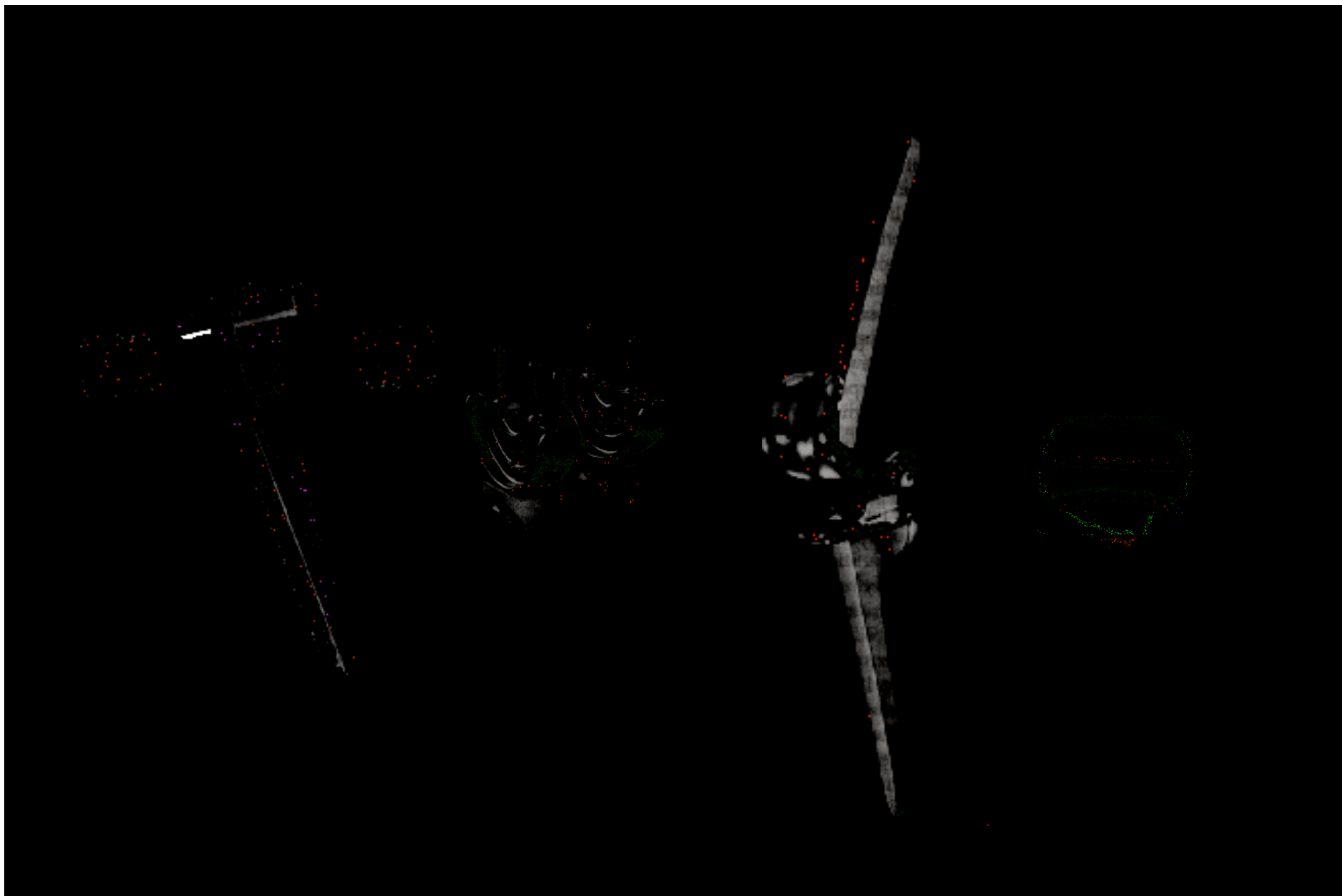
“Analysis of the first 25 patients suggests the total knee prosthesis of Irvine (UCI) design may be inserted without a need of more than average precision and technique. Despite a rather wide range of patient size, it is not necessary to have more than 1 prosthesis.”

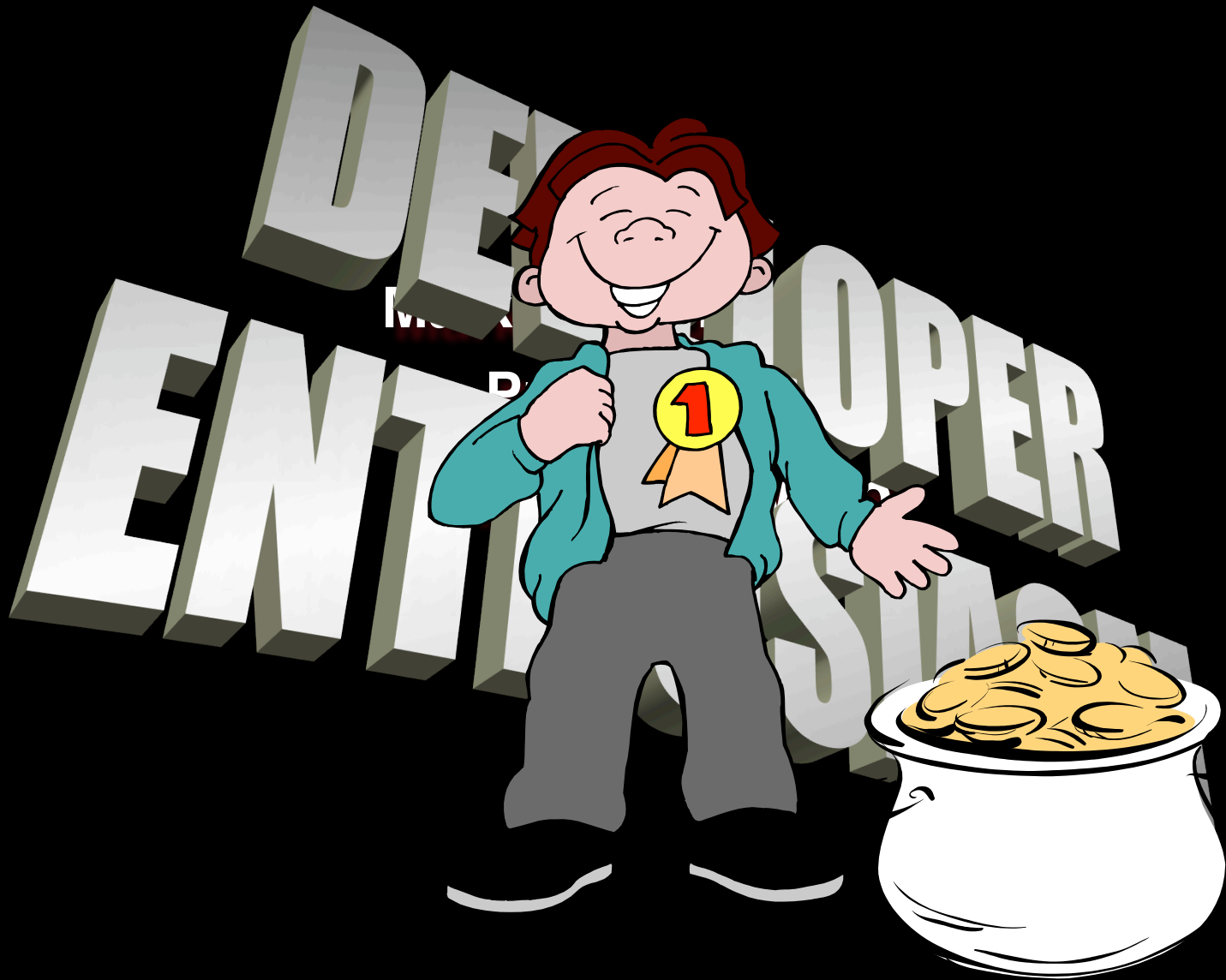
“The preoperative range of motion is generally exceeded. The average patient has been dramatically improved and the knee is almost always converted from a painful to a painless joint.”





**THE EVOLUTION
OF
TOTAL KNEE REPLACEMENT**





Developer Enthusiasm

Developer Enthusiasm

Distortion of Preliminary Data

Developer Enthusiasm

Distortion of Preliminary Data

- **Eliminate earliest cases (“learning curve”)**

Developer Enthusiasm

Distortion of Preliminary Data

- **Eliminate earliest cases (“learning curve”)**
- **Use subjective outcome criteria**

Developer Enthusiasm

Distortion of Preliminary Data

- **Eliminate earliest cases (“learning curve”)**
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Developer Enthusiasm

Distortion of Preliminary Data

- **Eliminate earliest cases (“learning curve”)**
- **Use subjective outcome criteria**
- **Short follow-up**
- **Bad outcomes are “lost to follow-up”**



Knowledge Finder® Search Formulation

1980 - 1998 OrthoLine®
[1999 Edition]



Search Progress
Search History 10 of 10

Free-Form Topic Search
loosening and total knee replacement

Emphasize Quantity | Relevance Filter | Emphasize Relevance

Boolean Search | Word Variants | Find Up To 1000 Documents | Sort By Relevance / Recency

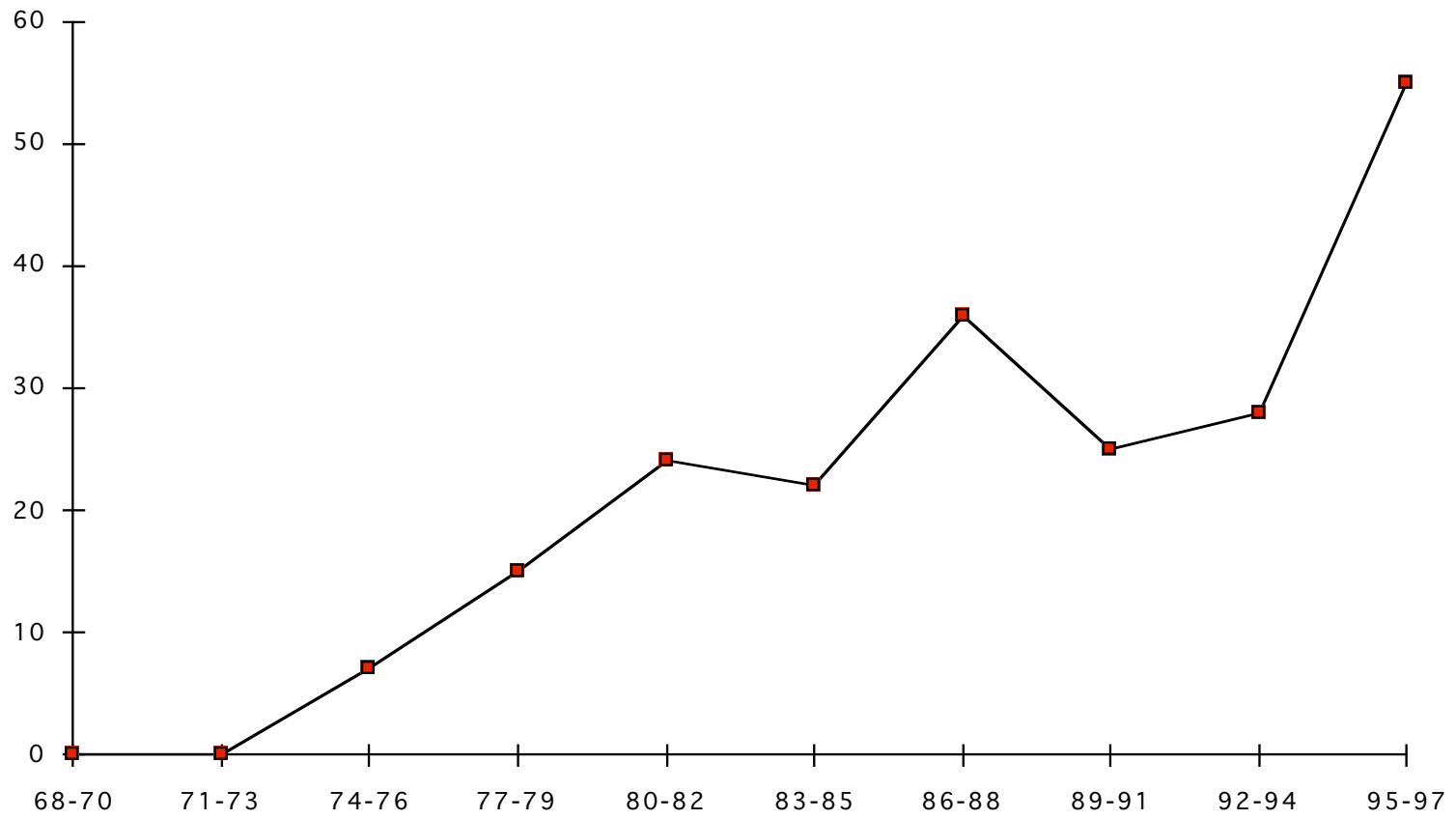
- Search Also/Instead By :
- MeSH® Thesaurus
 - Author Name(s)
 - Publication Date(s) ✓
 - Journal Title(s)
 - Publication Types(s)
 - Age & Subject Tag(s)

Reviews Only
 English Only

- Selected Dictionary/Thesaurus Search Terms
- ⊕ 1995 - All Articles (39539 Documents)
 - ⊕ 1996 - All Articles (40127 Documents)
 - ⊕ 1997 - All Articles (39226 Documents)

⊕ Use Only | ⊕ Try To Use | ⊖ Don't Use | Remove

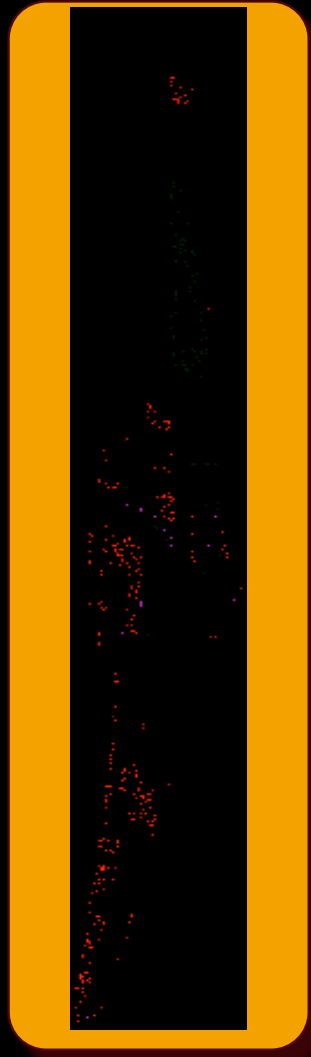
Number of Articles



“...we can expect all the earliest reports of a new design to be glowing and written by the designers and champions. When the longer-term empiric outcomes are less-than-rosy, the next wave of reports is written by individuals who are more objective because they are not directly linked to the design.”

“Because surgeons sell to other surgeons best, companies need surgeon champions who truly believe in the features of their products.”

Engl, CA: Pioneering in the First Century of Hip Replacement: Experiences of a Surgeon-Designer. Clin Orthop, 407, 35-49, 2003



HERBERT

**What was the government's role
In regulating the marketing of
such a device?**

NONE

How did the U. S. Government get involved in regulating medical devices?

Hypothesis 1: Government regulatory involvement is usually scandal driven.

Hypothesis 2: Magnitude of government regulations is directly proportional to the scandal's volume.

Hypothesis 3: The scandal's volume is directly proportional to the body count.

**1862 scandal: Civil War
dead from malnutrition &
starvation**

Body Count = 10,000s

**Bureau of Chemistry within
Department of Agriculture.**

**Scandal: Tainted Armour canned
meat to U.S. Army during Spanish
American War (1898-99)**

Body Count: Dozens

1905: *The Jungle*

1906: Pure Food Act

1931: Agriculture Appropriations Act
(Established FDA in Dept. of Agriculture)

1937: Massengill Scandal

(Sulfanilimide dissolved in diethylene glycol)

Body Count = 108

**1938: Food, Drug and
Cosmetic Act**

1962: Thalidomide Scandal

(Birth defects related to morning sickness pill)

Body Count = 20,000

1962: Amended Food, Drug and Cosmetic Act

(proof that product was both safe and efficacious)



1960s

FDA expanded the definition of drug to include devices

United States vs ...Bacto-Unidisk



“FDA..vital for the protection of public health...”“The term ‘drug’ had “a liberal construction consistent with the [1938] act’s overriding purpose to protect public health.”

Supreme Court, 1969

Late 1960s and Early 1970s Consumer Activism

1969: Environmental Protection Agency

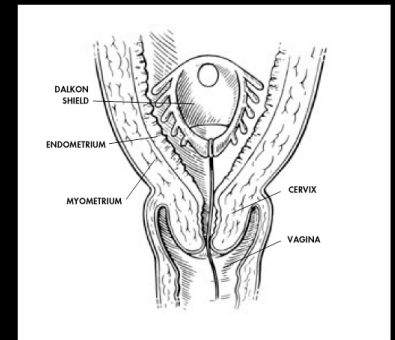
1972: Occupational Safety and Health Administration

1972: Consumer Product Safety Commission

1971: Dalkon Shield

Body Count = 2,100,000

1976: Medical Device
Amendments



1980s ORPHANS

- **Rare diseases (e.g. Gaucher's)**

1980s ORPHANS

- **Rare diseases (e.g. Gaucher's)**
- **Off label Use (e.g. Lidocaine bolus)**

1980s ORPHANS

- Rare diseases (e.g. Gaucher's)
- Off label Use (e.g. Lidocaine bolus)
- Rx for Fatal Disease (AZT for AIDS)

1980s ORPHANS

- **Rare diseases (e.g. Gaucher's)**
- **Off label Use (e.g. Lidocaine bolus)**
- **Rx for Fatal Disease (AZT for AIDS)**

1983: Orphan Drug Act

“It must come as an unhappy surprise to many to hear that, in 1989, we have no assurance that the medical devices used in, on, and around our bodies are safe.”

Congressman Henry Waxman, 1989

“The American device industry cannot be trusted”

Congressman Waxman

Body Count = 17,000

1990: Safe Medical Device Act

Civil penalties for underreporting adverse events during trials



- **National Childhood Vaccine Injury Compensation Program**
- **Pacemaker Re-imbusement Review and Reform Amendment**

2006: Vioxx/Bextra Scandal
(Cox-2 relative risks under-reported to FDA)

Body Count = 24,000

2007: FDA Amendments Act
(Increased post-Market Surveillance)

The FDA and the Medical Device Marketplace

F.D.A.

APPLICATION

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MARKETING

EXEMPT

- On Market Before 1976
- Class I
 - Testing Systems
 - Surgeons Gloves
 - Patient lubricants
 - Goniometers
- Class II
 - Jet Lavage
 - Wheeled Stretcher

EXEMPT

- Pre-1976
- Class I
- Class II



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**Application claiming the new device
is similar to products already on market**

510k NOTIFICATION

EXEMPT

- Pre-1976
- Class I
- Class II

**510k
Notification**



**Investigational
Device
Exemption**



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I.D.E. **(Investigational Device Exemption)**

- **Controlled clinical trial**
 - **Prospective & randomized**
 - **Limited number of investigators**
 - **Predetermined number of subjects**
 - **Adequate follow-up period**
 - **Meticulous data collection**
 - **Dedicated surveillance staff**

I.D.E. **(Investigational Device Exemption)**

- **Controlled clinical trial**
 - **Inst. Review Board approved**
 - **Extensive informed consent**

**Investigational
Device
Exemption**



NEW DEVICE

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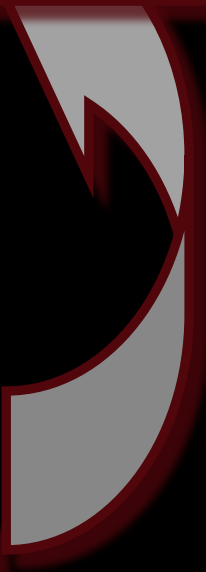
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**510k
Notification**

**Investigational
Device
Exemption**

NEW DEVICE



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EXEMPT
•Pre-1976
•Class I
•Class II

**510k
Notification**

**Investigational
Device
Exemption**

**P.M.A.
Pre-Market
Approval**

NEW DEVICE

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P.M.A. **(Pre-Market Approval)**

- **Must be proven safe & effective**
- **Panel of experts review data**
- **Approve or reject application**
- **Make suggestions for more data**

EXEMPT
•Pre-1976
•Class I
•Class II

**510k
Notification**

**Investigational
Device
Exemption**

**P.M.A.
Pre-Market
Approval**

NEW DEVICE

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EXEMPT
•Pre-1976
•Class I
•Class II

**510k
Notification**

**Investigational
Device
Exemption**

NEW DEVICE



**P.M.A.
Pre-Market
Approval**



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**G.M.P.
Good
Manufacturing
Practices**

G.M.P. **(Good Manufacturing Practices)**

- Labeling
- Manufacturing
- Packaging
- Storage
- Installing
- Servicing
- Training
- Auditing

EXEMPT
•Pre-1976
•Class I
•Class II

**510k
Notification**

**Investigational
Device
Exemption**

NEW DEVICE



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**P.M.A.
Pre-Market
Approval**

**G.M.P.
Good
Manufacturing
Practices**

**Post
Market
Surveillance**



Post Market Surveillance

Post Market Reporting

Post Market Tracking

Post Market Surveillance Studies

Some Permanent Implants (After Jan. 91)

Devices Subject to Postmarket Surveillance Studies Effective November 8, 1991.

- *Annuloplasty Ring**
- *Automatic Implantable Cardioverter Defibrillator**
- *Cardiovascular Permanent Pacemaker Electrode (Lead)**
- *Coronary Vascular Stent**
- *Implantable Pacemaker Pulse Generator**
- *Implanted Diaphragmatic/Phrenic Nerve Stimulator**
- *Replacement Heart Valve**
- *Total Artificial Heart**
- *Tracheal Prosthesis**
- *Vascular Graft Prosthesis (any diameter)**
- *Ventricular Assist Device - Implant**

Devices Subject to Postmarket Surveillance Studies Effective August 29, 1993.

- *Glenoid Fossa Prosthesis**
- *Implantable Infusion Pumps**
- *Implanted Cerebellar Stimulators**
- *Interarticular Disc Prosthesis (Interpositional Implant)**
- *Mandibular Condyle Prosthesis**
- *Total Temporomandibular Joint Prosthesis**

Effective, February 19, 1998, manufacturers will no longer be automatically required to conduct postmarket surveillance studies... Rather, FDA may order such studies...for any device:

- *the failure of which would be reasonably likely to have serious adverse health consequences; or**
- *which is intended to be implanted in the human body for more than one year**

IDE Testing

- **Limited number of patients**
- **Profit motive**
- **Marketing pressures**
- **Developer enthusiasm**

Developer Enthusiasm

Distortion of Preliminary Data

- **Eliminate earliest cases (“learning curve”)**
- **Use subjective outcome criteria**
- **Short follow-up**
- **Bad outcomes are “lost to follow-up”**

Search PubMed for schiffman BAK

Limits

Preview/Index

History

Clipboard

Details

Display AbstractPlus

Show

20

Sort By

Send to

All: 1

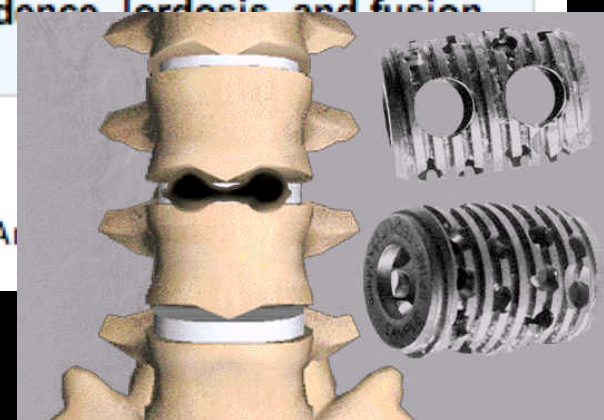
Review: 0

 1: [Spine J.](#) 2003 Sep-Oct;3(5):377-87.

Bilateral implantation of low-profile interbody fusion cages: subsidence, lordosis, and fusion analysis.

[Schiffman M](#), [Brau SA](#), [Henderson R](#), [Gimmestad G](#).

Spine Care Orthopaedic Professionals, 8610 Sepulveda Boulevard, Los Angeles, CA



71 patients

75% satisfactory results

composite scores were within normal range of the US population that has experienced back pain or sciatica. CONCLUSION: Bilateral implantation of low-profile cages in this patient population led to satisfactory outcomes. Subsidence and changes in lordosis were minimal. Fusion rates were good, especially for one-level cases. Patient satisfaction was relatively high, considering the population consisted of 96% worker's compensation cases. With proper surgical technique, bilateral low-profile cages can be used effectively to treat patients with degenerative disc disease.

25% + 32%

57% unsatisfactory results

Marketplace Experience

- **Unlimited number of patients**
- **Clinician skepticism**
- **Profit motive reduced**
- **Longer follow-up**
- **Expectation pressures**

Market Testing

Nature finds the hidden flaw

EXEMPT

- Pre-1976
- Class I
- Class II

**510k
Notification**

**Investigational
Device
Exemption**

NEW DEVICE



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**P.M.A.
Pre-Market
Approval**

**G.M.P.
Good
Manufacturing
Practices**

**Post
Market
Surveillance**

NEW PRODUCT NOTICE

This product is new; it has been tested according to FDA procedures and determined to be safe & effective. Unforeseen problems may become apparent with the passage of time that may limit the product's value or cause unexpected complications.

NEW PRODUCT NOTICE

This product is new; it has been tested according to FDA procedures and determined to be safe & effective. Unforeseen problems may become apparent with the passage of time that may limit the product's value or cause unexpected complications.

New Product Consent

Signed by doctor & patient

- **Acknowledge “New Product” status**
 - **Designed to overcome problems**
 - **Tested before marketing**
- **Discuss unforeseen problems**
 - **Low frequency not noted in PMA**
 - **Long-term problems**
- **Contact number of FDA**

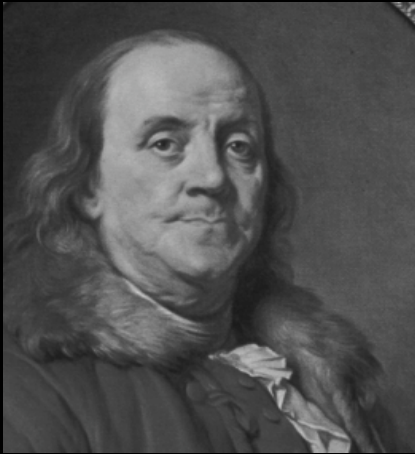
“NEW PRODUCT” STATUS

LIABILITY

“The social function of regulation depends on information—gathering data before marketing and reporting problems once the product has been distributed...The threat of liability intimidates producers... Thus, there are powerful incentives, even for responsible producers, to protect or withhold information.”

Susan B. Foote

Managing the Medical Arms Race



Dr. Benjamin Franklin



Dr. Thomas Bond

“I suspect there is more valuable knowledge in Physic to be learnt from the honest candid Observations of an old Practitioner, who is past all desire of more Business, having made his Fortune...

...and who by Experience has discovered
the Inefficacy of most Remedies and
Modes of Practice, than from all the formal
Lectures of all the Universities upon Earth.”

Benjamin Franklin

Feb 5, 1772



THE END