Electrical Stimulation of Bone: Present, Past, Future

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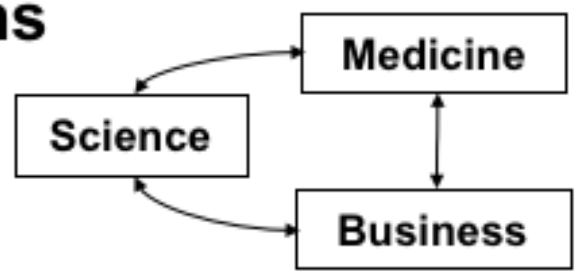
Summary

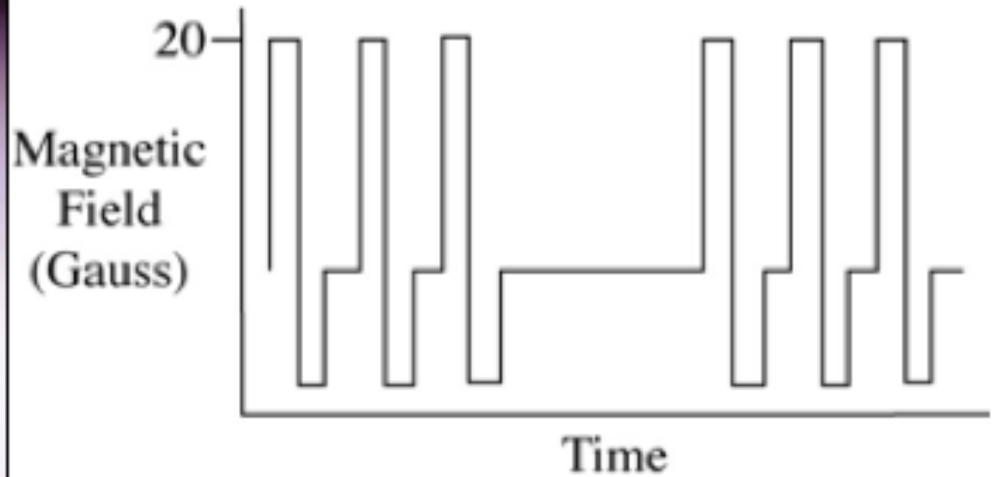
- **Describe available methods and indications**



- **History:**
- **Future in orthopaedics**

I'll describe the methods for stimulating bone growth that are in use presently, and the indications for which they are used. Then I'll briefly describe the most important historical factors that led to the availability of bone-stimulation systems that are presently in use. The history provides a good insight into the interaction between scientific, medical, and business considerations in the development a new treatment. Lastly, I'll briefly describe the outlook for the use of electrical stimulation in orthopaedics.

Electrical Stimulation: Magnetic Fields



One method of stimulating bone involves the use of magnetic fields. They are applied to the site to be treated using a coil (right) that is powered by portable circuitry (middle) that contains a rechargeable battery that is recharged when the unit is stored in its charger (left) during the portion of the day when it's not used by the patient. The most popular magnetic field device applies the field in the form of a complex pattern of spikes having a peak amplitude of about 20 gauss but a very small average magnetic field because the spikes have a very short duration.

Electrical Stimulation: Magnetic Fields

Nonunions

The original application for which magnetic fields were approved was the treatment of bone nonunions. It can be used on any bone except the flat bones and vertebrae. It can be used whether the nonunion is congenital or traumatic in origin.

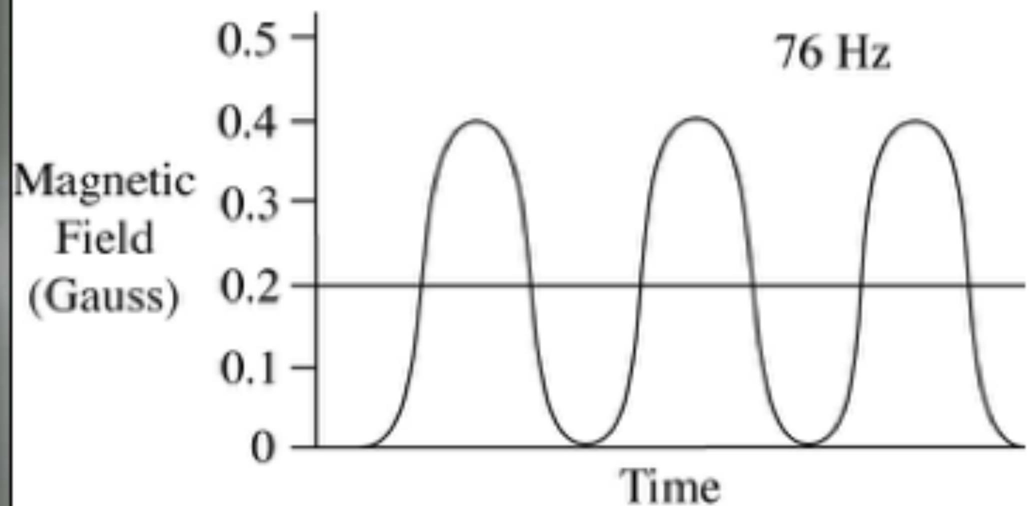
Electrical Stimulation: Magnetic Fields

- **Indication: Nonunions (trauma and congenital)**
- **Duration: Months; >10 hours/day**
- **Success Rate: 70%, more or less**
- **Drawback: Bulky, daily exposure time**

The fields are applied 8–10 hours per day. The devices available today are so compact and portable, for many nonunions they can be worn while the patient performs routine daily activities. Otherwise, the coils can be worn while the patient sleeps. Typically, it takes several months of treatment to re-initiate the healing response in the bones. The success rate is roughly equal to that achieved using surgery.

Electrical Stimulation: Magnetic Fields

Spine Fusions



This is a magnetic field generator made by another company. It can be used to treat nonunions, and also as an adjunctive treatment in spinal fusions. In the latter case, after the surgeon performs the surgery magnetic field stimulation is used during the healing period to increase the success rate for fusion. The magnetic field applied to the patient is quite different compared with the field depicted previously, but the expected clinical results are essentially the same, showing that the details of the magnetic field are not critical.

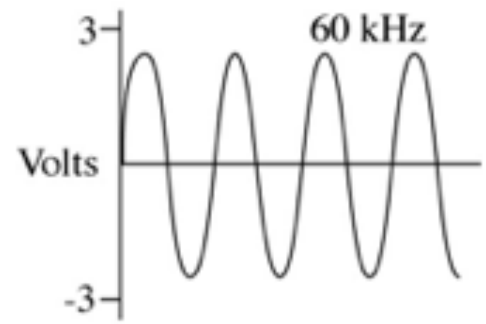
Electrical Stimulation: Magnetic Fields

Spine Fusions

- **Indication:** **Adjunct for primary lumbar spinal fusions (1 or 2 levels)**
- **Duration:** **30 minutes/day**
- **Success Rate:** **20-30% increased fusion rate**

Spinal fusions typically have success rates of 50-60%. The addition of magnetic field stimulation can elevate the success rate 20–30 percentage points higher. This application of magnetic field stimulation was established as efficacious to the satisfaction of the Food and Drug Administration many years after they accepted the idea that magnetic fields could bring about healing of nonunions. In the intervening years it became clear that there was really no need to treat a site for 8-10 hours a day, and in successive clinical studies the treatment time was lessened to the point where today it is only 30 minutes a day. Unlike ordinary scientific practice where results of one investigator are published and are available for the use of all others, the Food and Drug Administration adopted the odd practice of doing exactly the opposite. Consequently, even after it is demonstrated by one manufacturer that 10 hours' exposure is unnecessary and 30 minutes' treatment is sufficient, the manufacturer saddled with the 10-hour stipulation cannot sell its device for use at the shorter time period unless it conducts a full-blown clinical study to reprove the proposition that had been proved previously. If manufacturers do not perform duplicate studies, which they often don't do because of the great costs involved, they remained saddled with the unnecessarily long exposure times.

Electrical Stimulation: AC Current



AC current is also an approved electrical modality for treating bone. The current is applied by means of two electrodes quite similar to EKG electrodes. They are arranged on the skin so that the current path traverses the site to be treated. The current that flows under conditions pertinent to this device are below the level of sensation, thereby permitting the currents to be applied more or less continuously.

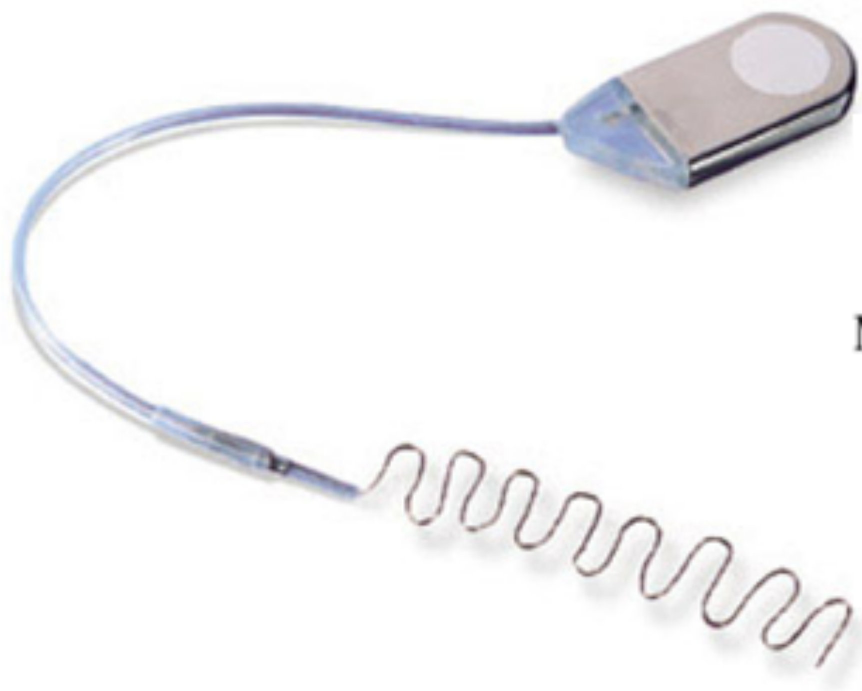
Electrical Stimulation: AC Current

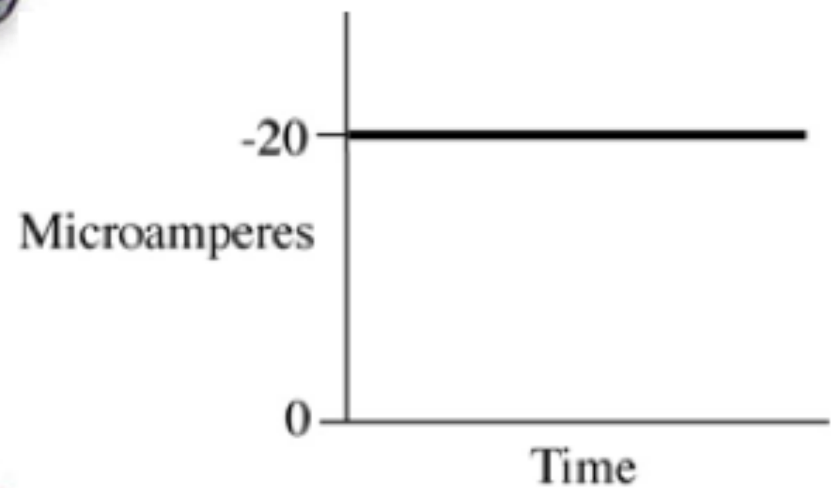
- **Indications:** **Nonunions** **(excluding vertebrae and flat bones)**
- **Duration:** **Months**
- **Success Rate:** **80%, more or less**
- **Drawback:** **Patient cooperation**

AC current is approved for the treatment of nonunions. It is a slow-acting form of therapy, and typically requires several months to bring about healing. When the electrodes are applied properly and diligently, healing rates equal to magnetic stimulation (and surgery) can be achieved. The great drawback with the AC method is the need to change the electrodes daily. The advantage is that the circuit that produces the current is quite small and easily portable.

Electrical Stimulation: DC Current

Nonunions

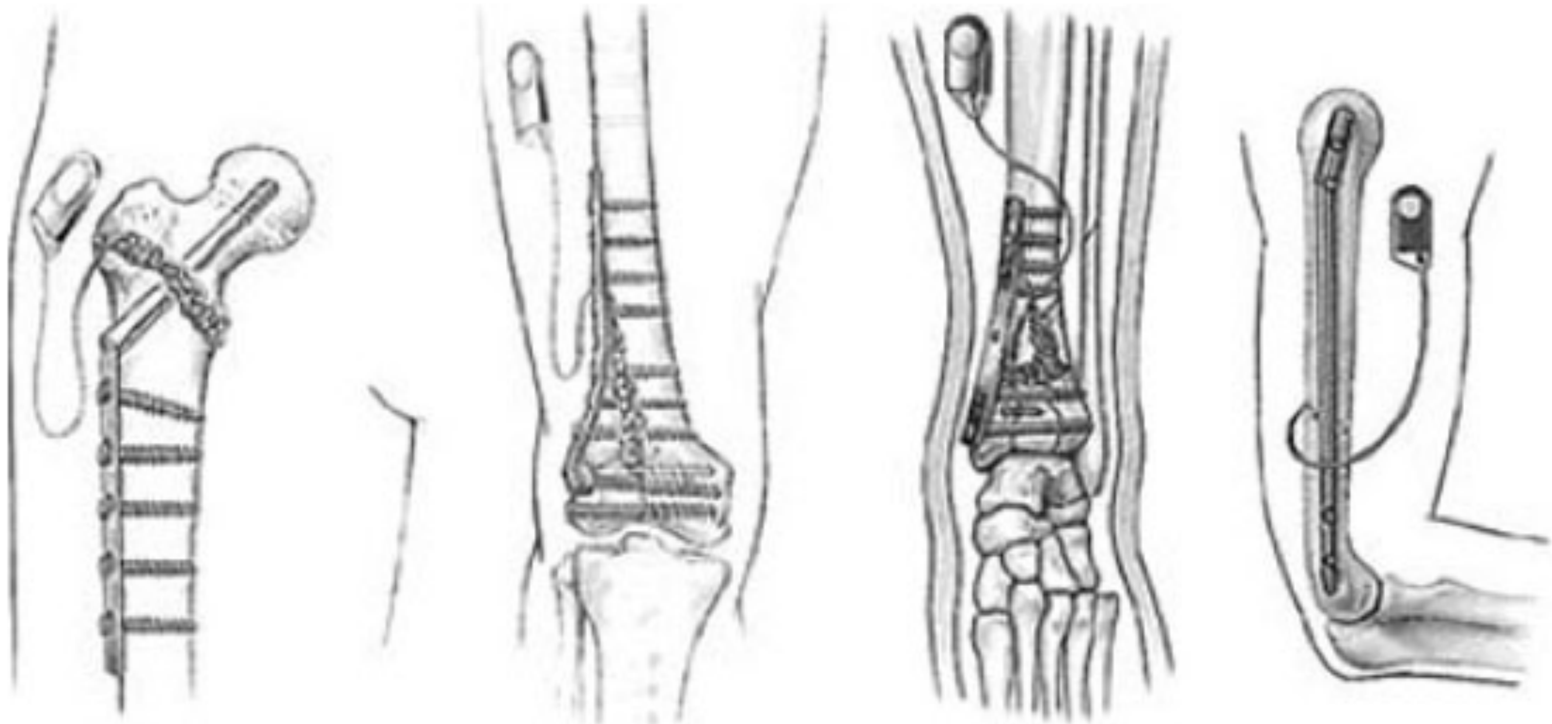




The third type of electrical device in use today for stimulating bone is a device that supplies DC current to the treatment site. The device consists of a titanium cathode that is placed directly in the nonunion during a surgical procedure, and an anode formed by the metallic shell of the circuitry that produces the current. The anode is placed in a pocket in soft tissue. The device is designed to produce 20 microamperes of current, at most. During the healing process the bone envelopes the titanium cathode, permanently sequestering it in bone. The anode, together with its lead wire are removed during a second surgery that is performed after healing is complete.

Electrical Stimulation: DC Currents

Nonunions



TOTALLY IMPLANTABLE SYSTEM

The totally implantable system, when used for nonunions, is typically employed to stimulate healing in severely traumatized bones.

Electrical Stimulation: DC Current

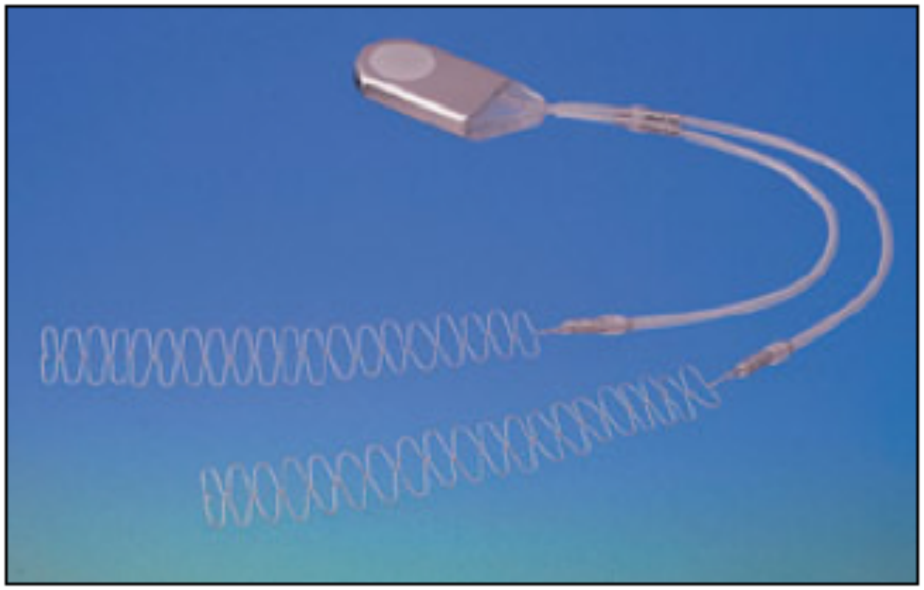
Nonunions

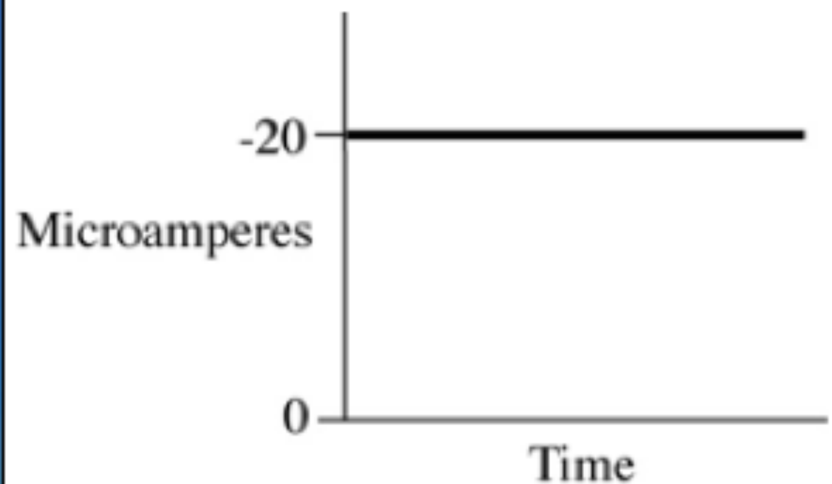
- Indication: Long bone nonunions. Adjunct to I/E fixation or graft
- Duration: Months
- Success Rate: 50%, more or less
- Drawback: Two surgeries needed

The success rate of the total implantable system is difficult to ascertain because it is often used as an adjunctive treatment, typically in severely injured bones. Its use involves two surgeries, but in applications where it is used as an adjunct the initial surgery is usually motivated by orthopaedic considerations involving reduction and fixation at the injury site.

Electrical Stimulation: DC Current

Spine Fusions





A DC current is used more commonly as an adjunctive treatment in spinal fusions. If the fusion is performed at two levels, the device employed has two cathodes so that the current output is distributed to the two levels where the fusion is desired.

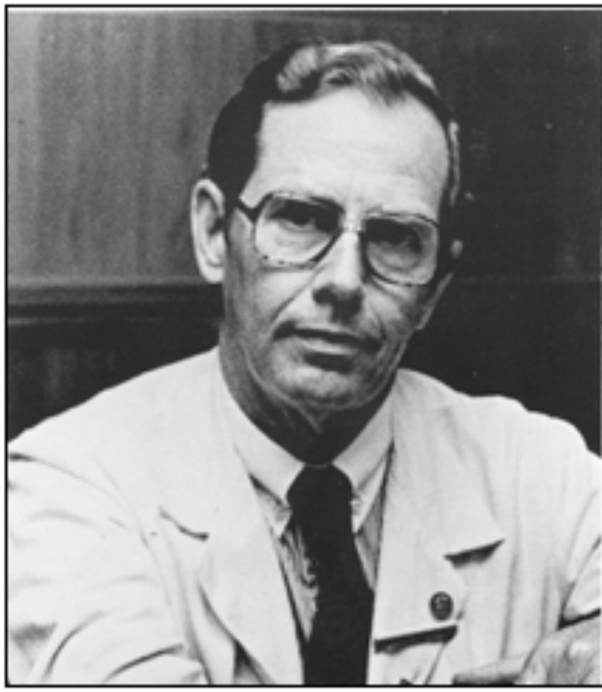
Electrical Stimulation: DC Current

Spine Fusions

- Indication: Spinal fusion adjunct
- Duration: 26 weeks
- Success rate: +27% (54% → 81%)
- Drawback: Surgical removal of circuit

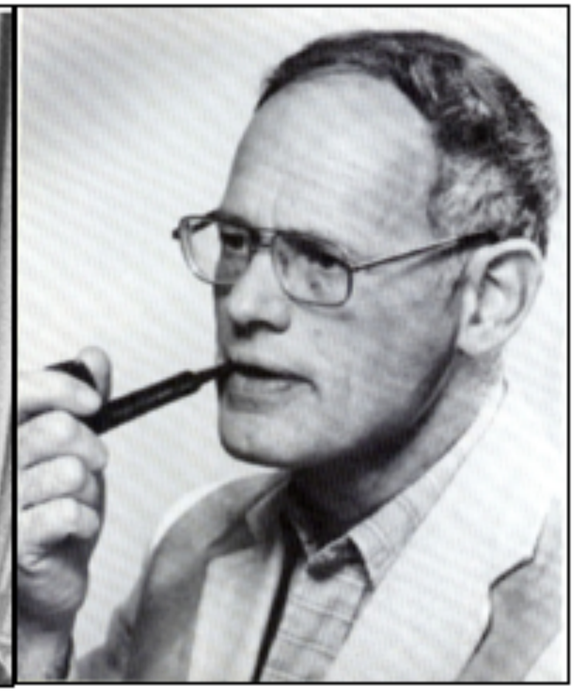
The efficacy of DC current for promoting spinal fusions is more or less well established.

Pioneers of Electrical Stimulation



C. Andrew Bassett, M.D.
Columbia

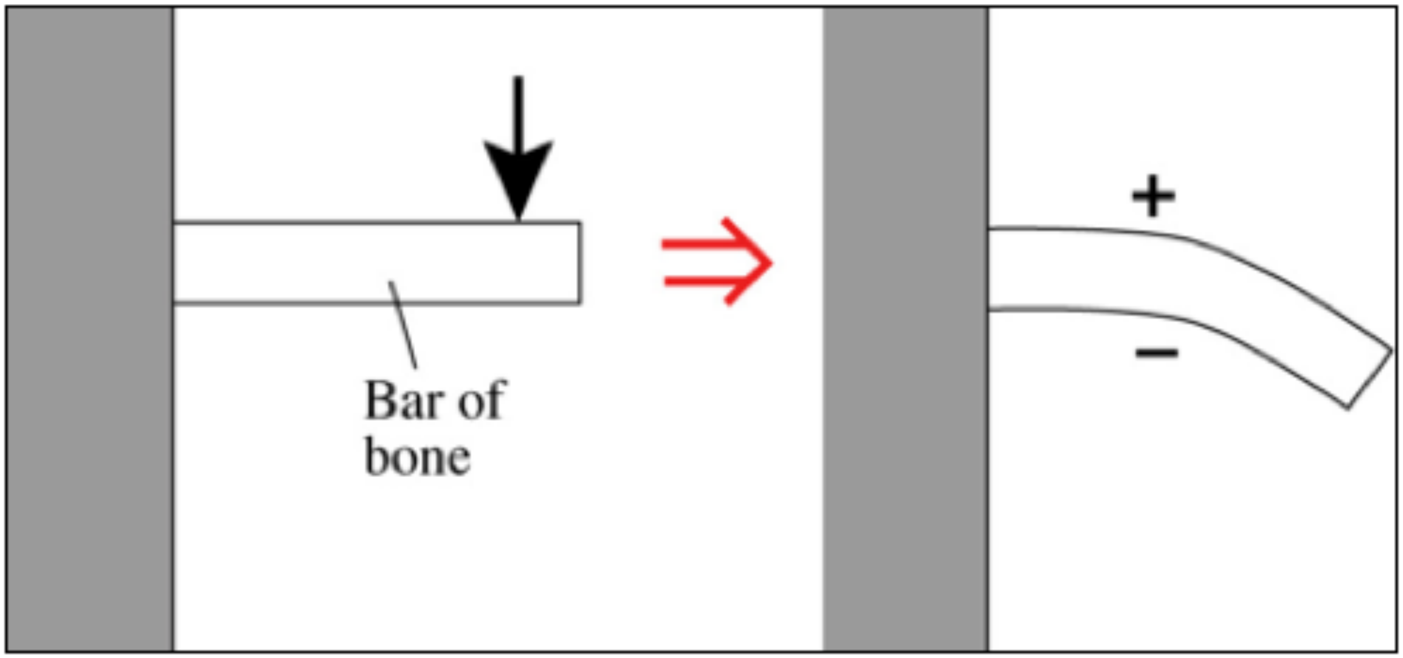
Carl Brighton, M.D.
University of
Pennsylvania



Robert O. Becker, M.D.
Upstate Medical Center
(VA Hospital)

These are the men who originated the idea of using electrical energy for stimulating bone growth. Their goals were different from one another and their interactions were complex. Their work is interesting because of the impact it had on orthopaedic treatments, but even more interesting because of the insight it provided into the way orthopaedic devices were developed.

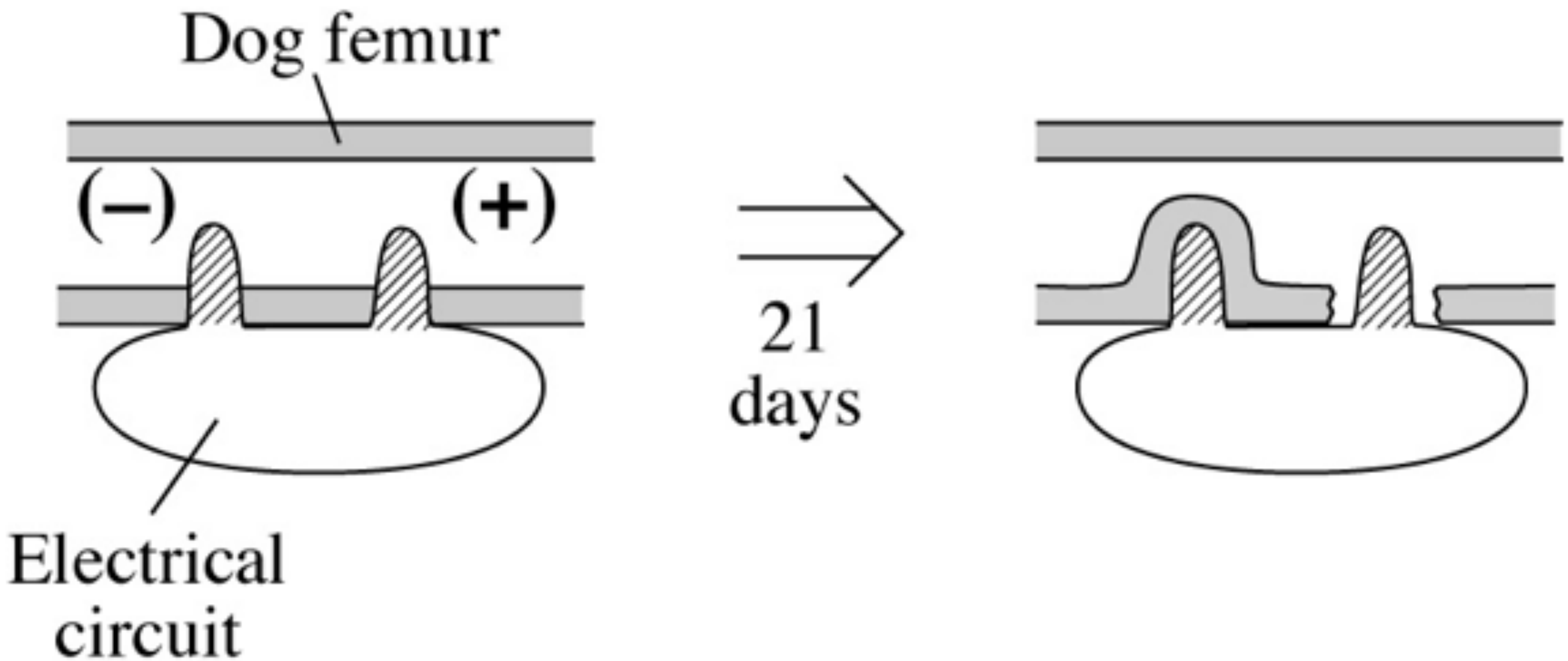
First Seminal Observation*



*1961, Bassett and Becker

Othopaedic bioelectricity began in the early 1960s following publication of two seminal experiments. Its heyday was in the 1970s and 1980s when many hundreds of papers were published in basic science and clinical journals. Today, the fashion for attempting to stimulate bone cells involves the use of ideas that are even older than bioelectricity (at least in the 20th century) such as bone morphogenic protein.

Second Seminal Observation*



***1961, Bassett and Becker**

The second important experiment involved implanting battery powered circuits in dogs and assessing the effect on bone growth 21 days later. Two holes were drilled into the medullary canal to accommodate the anode and cathode of the circuit, resulting in a current flow directed generally along the endosteal surface. The result, assessed qualitatively, was a massive amount of bone growth at the cathode and bone resorption at the anode. These experiments were interpreted to indicate that bone grew in response to negative electricity, which was the hypothesis that was suggested by the piezoelectric experiments. By the time these ideas were recognized as being great oversimplifications, developments within orthopaedic bioelectricity had led to uncritical acceptance of the simple ideas, and consequently the more mature perspective was never able to gain a foothold.

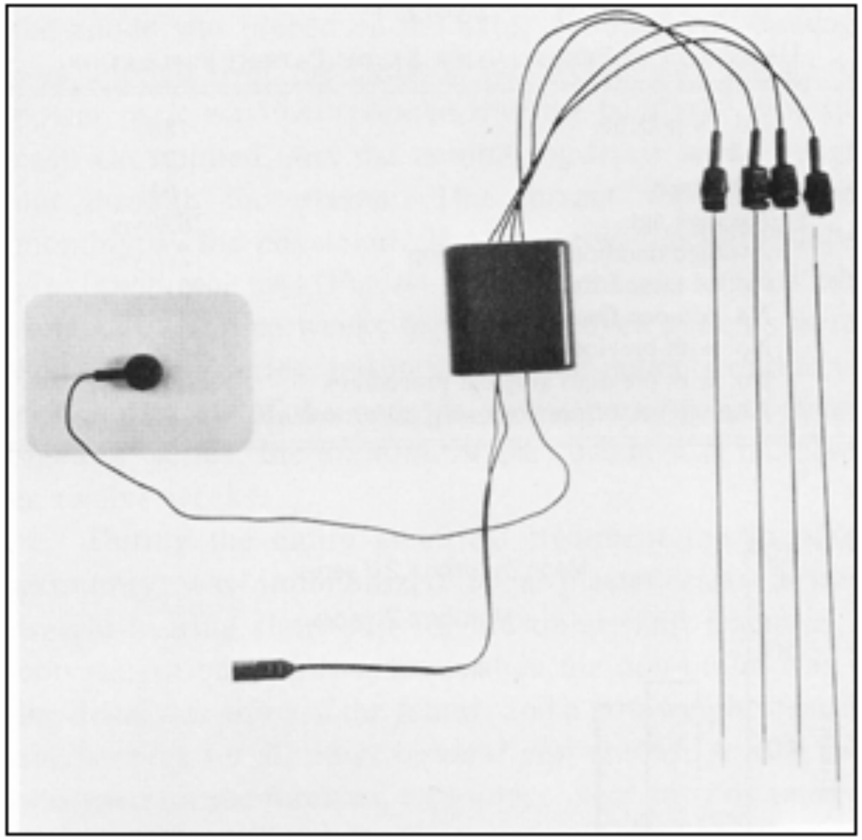
Electrical Stimulation of Bone

Methods and Applications

	METHOD	APPLICATION	THEORY	COMPANY
Brighton	Percutaneous negative electricity Transcutaneous AC electricity	Nonunions	O_2	Zimmer Bioelectron
Bassett	Magnetic fields	Nonunions	Ca^{2+} influx	Electrobiology (EBI)
Becker	Positive and negative electricity	Infected nonunions	Nonspecific Iontophoresis	Ritter
Dwyer (Australia)	Totally implantable system	Spine fusion adjunct		

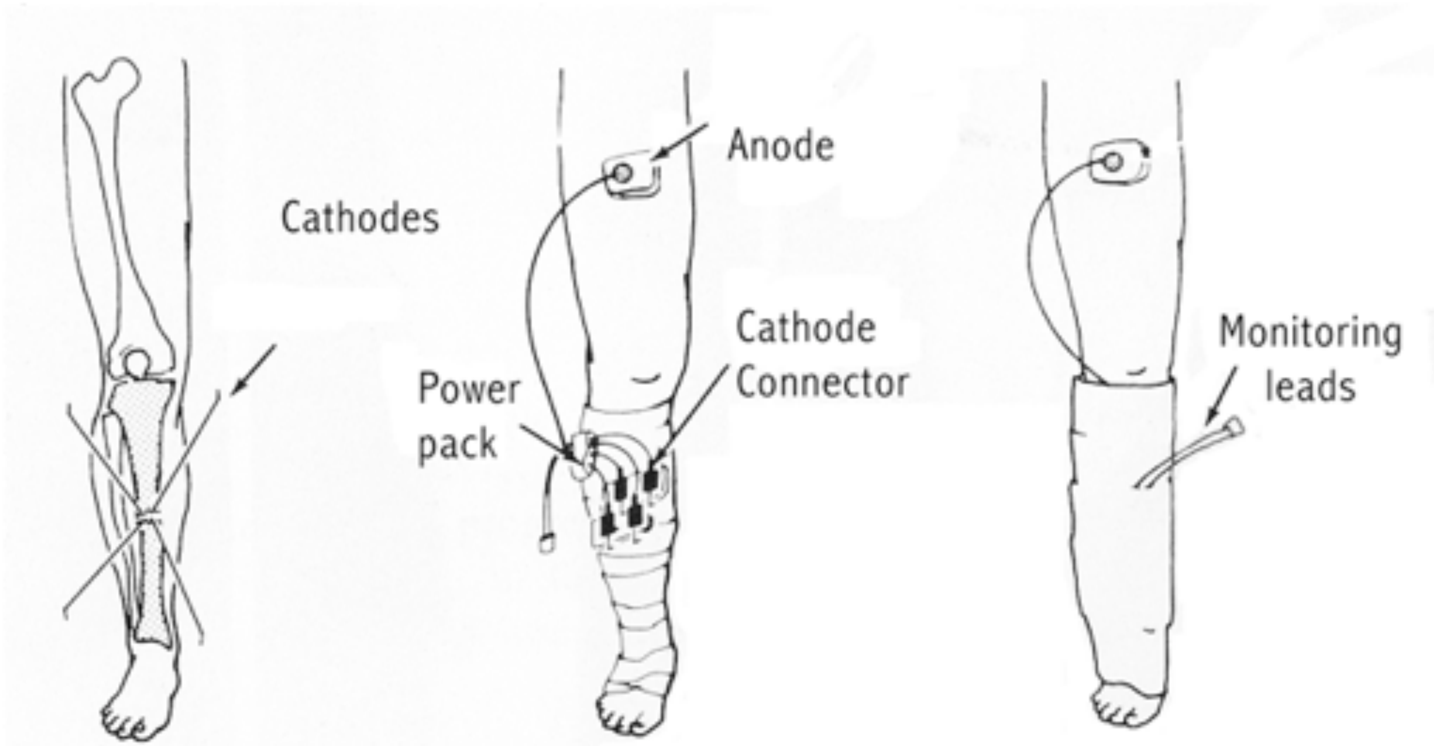
Four investigators and five different electrical systems developed in the years following the seminal observations. Each system drew its theoretical justification from the earlier work, but the systems differed markedly regarding the concrete device that was hoped would be capable of producing efficacious results in patients. Brighton developed two methods and Bassett and Dwyer each developed one method, and three of these four methods survived to the present day. Becker's method never reached the market.

Brighton’s Negative Electricity System



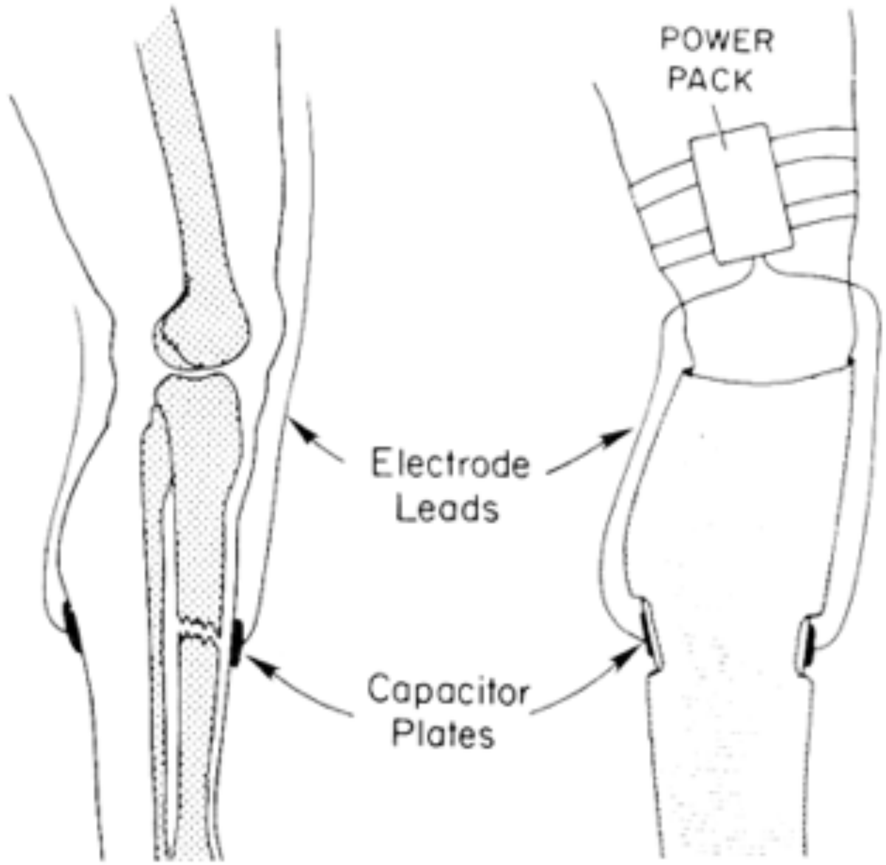
Brighton’s first method consisted of placement of cathodes (four shown on the right) at the nonunion site. Stainless-steel wires were drilled into the site percutaneously and attached to a battery powered circuit that was positioned somewhere on the cast. The anode (the return electrode for the current) (left) which was similar to a grounding electrode used on patients during surgical procedures, was placed on the skin. The lead from the circuit (middle, bottom) permitted measurement of current flowing in the bone.

Brighton's Negative Electricity System



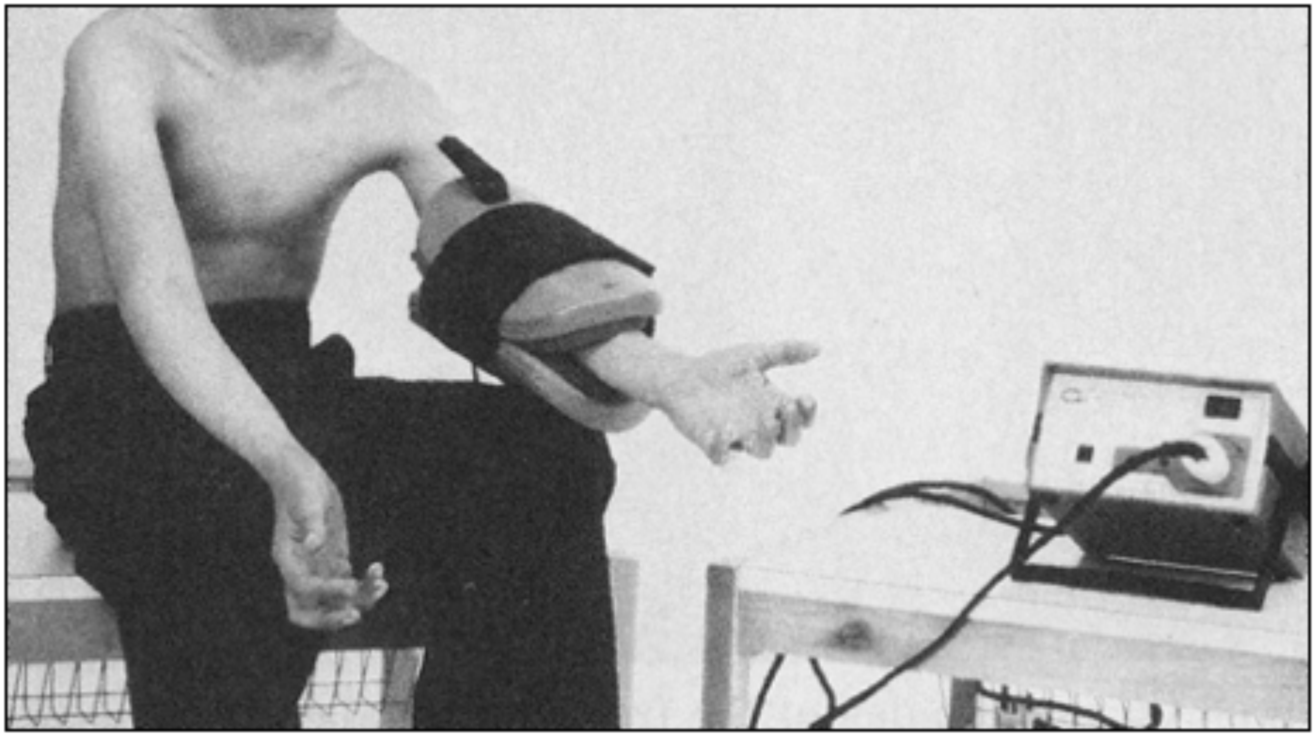
This slide depicts a typical application of the system to a nonunion in the tibia. Despite the engineering sophistication of the system, and its efficacy, it failed in the marketplace because of resistance from both patients and orthopaedic surgeons.

Brighton's AC System



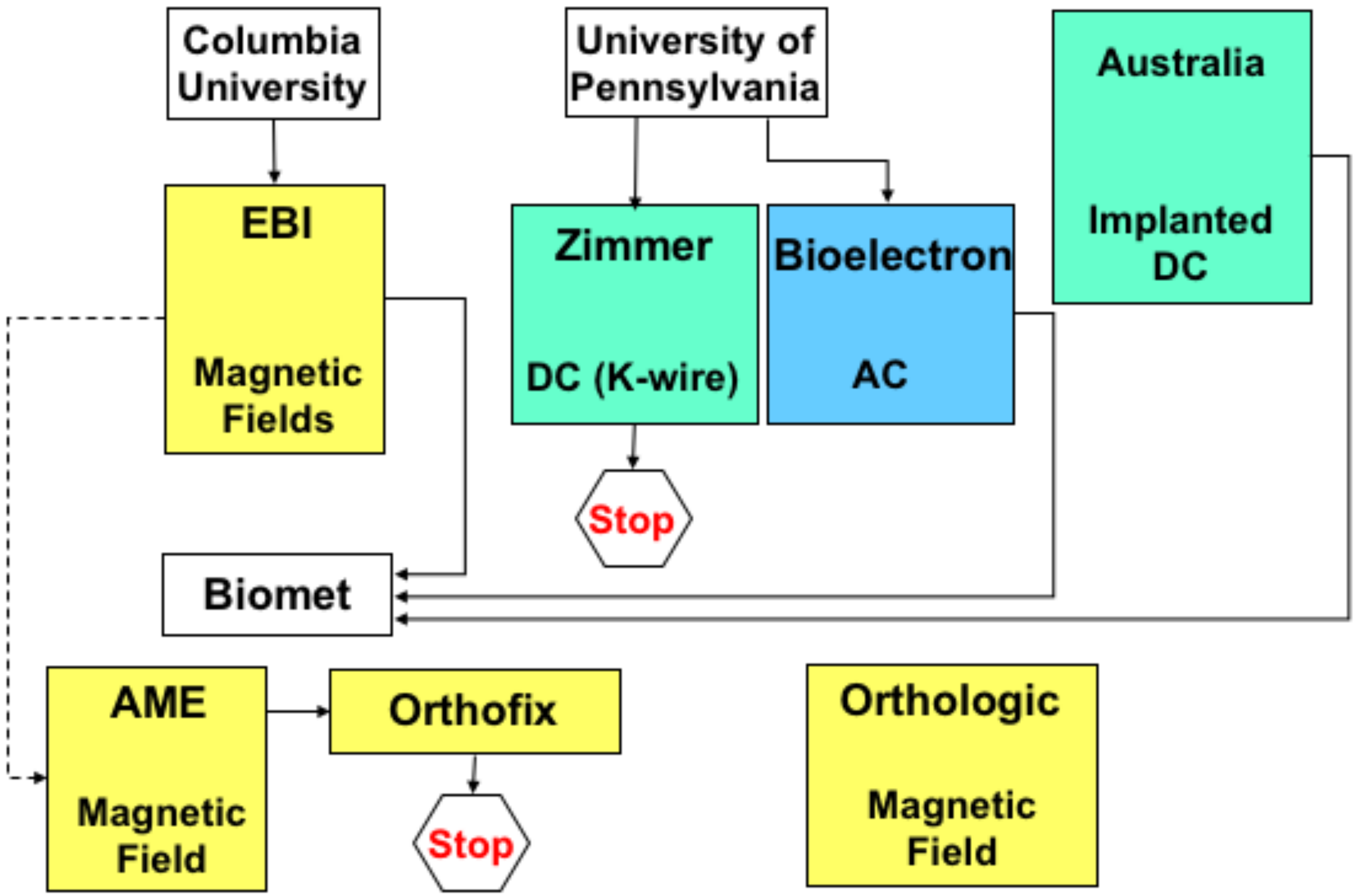
Brighton believed that the marketplace resistance was based primarily on the need to perform a surgical procedure (transcutaneous insertion of the cathodes). Consequently, he developed the AC system, which required no surgery for its implementation. This system is presently on the market.

Bassett's Field System



The initial magnetic field system developed by Bassett involved the use of relatively large coils that were powered by a device that was plugged into a wall outlet, thereby severely limiting patient mobility. Over the years the coils and the device that powered them became smaller and lighter. These modern designs are in use today.

History of Bone Stimulation Companies



For the most part, today, for the orthopaedic surgeon, the use of bone stimulation is essentially a matter of one-stop shopping. Essentially all of the important companies in the bone stimulation business were eventually acquired by Biomet.

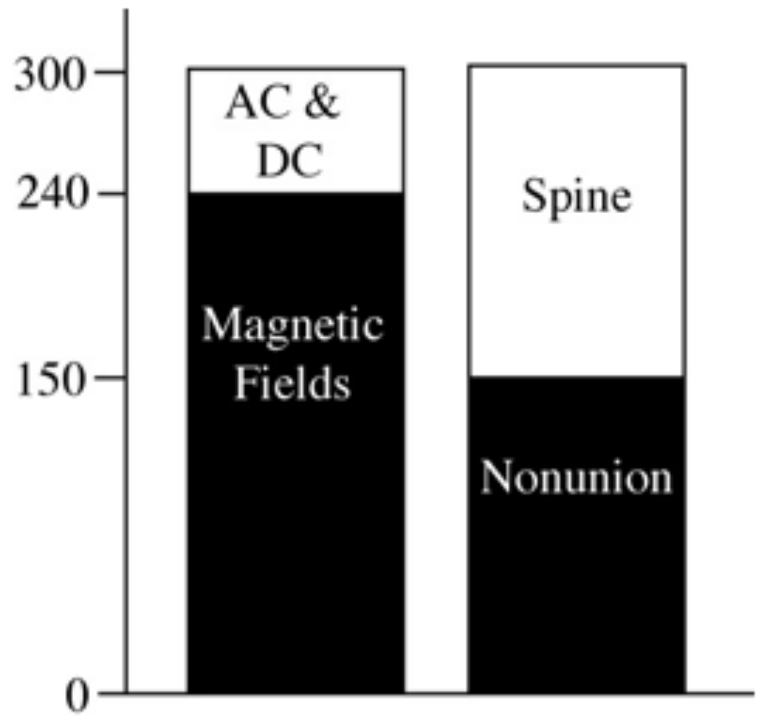
Worldwide Orthopaedic Device Market $millions)

SEGMENT	1998	2002	COMPOUND AGR
Reconstructive	4,090	5,400	+7%
Trauma	1,166	1,60	+9%
Spinal	950	2,300	+25%
Arthroscopy	700	1,100	+10%
Sports Medicine	540	800	+10%
Bone Cement	250	320	+6%
Bone Stimulation	**136**	**190**	**+9%**
Bone Subs & Orthobiologics	107	500	+47%
Ancillary Products	1,098	1,300	+4%

Source: Merrill Lynch Estimates

The worldwide orthopaedic device market in 1998 was about $10 billion of which $136 million consisted of bone stimulation devices. The projected increase of bone stimulation business was such that the volume of about $190 million dollars was expected for last year. That turned out to be an underestimation.

Bone Growth and Spinal Fusion Stimulation U.S. Market 2002 ($ millions)



Last year the U.S. market alone was about $300 million, the overwhelming majority of which involved the use of magnetic fields. Their use as an adjunct in spine surgery is increasing significantly, and now represents about 50% of the applications of bone stimulation. It seems likely that it will eventually become the most frequent indication for the use of bone stimulation. The data is from Frost and Sullivan estimate.

Electrical Stimulation of Bone: Present Applications

• Nonunions	OK
• Spinal Fusion	OK
• Accelerate Fracture Healing	X
• Osteoporosis	X
• Avascular Necrosis	X
. . .	?, but I doubt it*

* Because nobody knows how it works

The pioneers of bone bioelectricity developed the applications for nonunions and spinal fusions. When their work was taken over by the companies, all meaningful research stopped and no further applications were ever developed. The companies sponsored numerous clinical trials aimed at testing whether the signal that they owned was efficacious for treating any of a wide variety of orthopaedic diseases. These attempts were essentially based on hopes, not science, and not surprisingly they all failed.

Conclusion

- **Electrical stimulation has bona fide applications (small but stable market).**
- **Don't believe <u>anything</u> you read about how it works.**

Very little concerning the basic science of electrical stimulation of bone has been published since 1961 that is worth reading today. The good news is that the technique works and is efficacious, particularly in spinal fusions where, for relatively little extra cost, the likelihood of success of a procedure can be enhanced markedly. The bad news is that the basic mechanisms involve stimulating bone cells with electricity are completely unknown, and consequently the potential of the method for treating other diseases, not only bone diseases, is not susceptible to rational evaluation.