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Medicine  Health  
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**Biohybrid Limbs**

**A CME Issue**

# What's in a Name???

GOOD - authentic, honest, just, kind, pleasant, skillful, valid

NEIGHBOR - friend, near

ALLIANCE - affiliation, association, marriage, relationship

CORPORATION - company, business establishment

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## Commentaries

### Dress Codes for Doctors

**THERE ARE TWO PARTS TO THIS COLUMN.** The first is my reflection on dress codes, and the second is my reflection on someone else's reflection on dress codes.

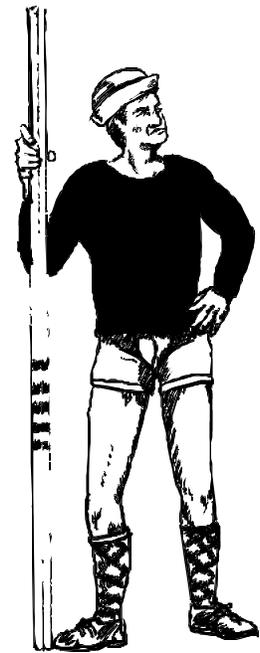
My medical school training emphasized a strict dress and behavior code. Neither students nor doctors were allowed to drink beverages or eat in front of patients. All adult patients were called Mr., Miss or Mrs. (before Ms was coined). Medical students and house-officers always wore white coats. Men wore ties. Coats and ties were required regardless of the temperature. At that time the hospitals were not air-conditioned so that the wards in Manhattan during the summers were hot and uncomfortable. And the end rooms on most wards were large, with 12 beds. It was not pleasant. Interestingly I didn't rebel. I always wear a tie when I see patients (except on weekends). I feel uncomfortable if a medical student or resident working with me is not wearing a tie and a white jacket. It has been imprinted on me that this dress is a token of respect, not for the profession, but for the patient. It's true that I don't always wear my white coat. I usually do, but in my private office, with my bald head, gray temples and gray beard, I can compensate somewhat by the "gravitas" of age. But my students can't.

During my training I rotated through city hospitals. It was there that I believe the dress code should have been enforced the most, and was actually followed the least. It is in these bastions of the poor and the oppressed where the patient needs to be treated with the respect *they* desire, not the dress down attitude that suggests social identification. The casual attire that is meant to indicate unity with the oppressed, that dress codes don't matter, that we're all in this together and are all equal, actually are often interpreted as a sign that "real" doctors, like the ones on TV catering to rich people, don't work at the city hospi-

tals, that these hospitals are for trainees who aren't good enough for the voluntary hospitals and they reflect their poor quality with their insensitivity by "dressing down."

This isn't a problem in Rhode Island as it is in the big cities. But a more challenging problem that I have noticed, albeit rarely, is the female student who dresses in a manner I deem thoughtless. In fact, the only house-officer whose dress I've ever complained about was male. I found him making rounds on a weekend wearing blue jeans and a t-shirt. I talked to his chair who threw up his hands and said he'd already talked to the young man and there wasn't anything he could do. After all, it didn't make sense to threaten to remove him from the program for determined minor social maladjustment. A second dress problem I heard about, was a neurology attending many years ago who refused to wear a tie or white coat, and kept his shirt unbuttoned, exposing his hairy chest. The chair of another department told him he was forbidden from entering his wards to see patients there, even to recruit them for his studies, unless he dressed better. The neurologist chose to not change. He doesn't work in RI any more.

The *New York Times* ran a column recently, written by a woman physician, describing the conflict she felt when a male colleague asked her to talk to a female house-officer about her mini-skirt and low blouse. The male physician was astute enough to realize that he shouldn't be talking to the resident himself, but the female colleague was herself very uncomfortable about confronting the resident, and, in fact, chose not to do it. I was sympathetic to them both. I had had the same problem with a student. In my case, luckily, it was a high school student doing a research project. She was so young that I was able to inform her about my dress code without causing a problem. If she



had been a medical student or house-officer, I wasn't sure how'd I handle it. The problem gave me pause. I thought I'd probably ask some older female professional to talk to the involved student, just as the *N Y Times* article described.

So, imagine my surprise at Thanksgiving, when my medical student daughter announced her letter to the *NY Times* decrying the bigotry of the very article about dress codes that I had identified with so closely (both the article and the dress codes). Luckily for me she declaimed before I did, so I knew where to stow my opinion. I marveled both at how different the two ends of the gender and age spectrum looked at things, and at how smart and independent a thinker my daughter had become. (She never reads what I write so my comments are safe here).

I am therefore stuck with a dilemma. My training, my hard wired inner core, tells me that male medical students should wear clean white jackets and ties and be either clean shaven or bearded but not in-between and women should dress relatively modestly. On the other hand, my demurely dressing daughter tells the world, "break out the defibrillators" because women doctors can't be told how to dress, and if they want to wear mini skirts and bear their midriff, they won't be stopped.

I know now that I, at least, won't be stopping them.

— JOSEPH H. FRIEDMAN, MD

# Perils of Life In the Left Lane

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**WHAT DO MICHELANGELO, MARTINA NAVRATILOVA AND MARILYN MONROE HAVE IN COMMON?** Certainly enduring fame and the fact that they all possess given names beginning with the letter M. But further, all three are left-handed, a biological characteristic that they share with about 10% of the human population.

It should not come as a surprise, then, if about one-tenth of the world's famous folk are left-handed. The critical question really is whether left-handedness is merely a bland, neutral attribute or alternatively, whether it confers measurable qualities—strengths or weaknesses, abilities or vulnerabilities, positive or negative properties—upon those endowed with this characteristic?

The most obvious of the many positive biological traits is longevity, the ability to live longer than others in the same era and the same community. By this criterion it appears that the right-handed live longer. About 10% of the total population is, on average, left-handed, although this frequency diminishes progressively with age. Thus, about 13% of youngsters are left-handed but beyond the age of 80 this percent drops to about 1%. Lefthanders, as many emergency rooms will inform you, are more prone to accidents [both industrial and vehicular], possibly because they live in a world where most tools and kitchen contrivances are designed for right-handers. Researchers have also noted that autoimmune diseases and various psychoneuroses seem to be more common in lefthanders. On the other hand, lefthanders seem to recover more readily from the disabling effects of stroke and are less prone to become aphasic following brain damage.

These biological factors favoring right-handers pale to insignificance when compared with the cultural prejudice against left-handedness. Consider the semantics of the words left and right. In English, the word right signifies correctness [the right thing to do], laudable stature [uprightness], ethical correctness [knowing right from wrong], inalienable entitlements [Bill of Rights], inherited privileges [birthrights], rationality [he's not in his right mind], legitimacy [the divine right of kings] as well as factualness, accuracy, dexterity [from the Latin, *dexter*, meaning on the right hand] and adroitness [from the French, meaning on the right]. Left, on the other hand [Ah, but which hand?] usually connotes clumsiness, awkwardness, lameness, out of step [left-footed], tardiness [left behind], something twisted [a left-handed compliment] or evilness [the Latin word for left is *sinister*].

Thus there are both biological advantages and disadvantages to being left-handed; but in a world mildly hostile to lefthanders [in some cultures where left-handedness is a satanic sign, left-handed children are routinely punished], the right-handed majority manages to survive somewhat longer.

With the odds slightly against them, how have the lefties prospered in this competitive world? Until James Garfield was elected in 1880, no American president had been left-handed. Since 1928, however, six of the 13 presidents [46%] have been southpaws [Hoover, Truman, Ford, Reagan, G.H.W. Bush and Clinton]. Perhaps, in a world of increasing chaos, so much veering toward left-field, that this nation turns to those lefties who

see things differently [an anonymous observer declared that lefties perceive the right-handed world as though viewed through a mirror]. Two of the current nine Justices of the Supreme Court [Kennedy and Ginsburg], incidentally, are also left-handed.

Many world leaders of the past have been said to be left-handed, especially those who excelled in military conquest. These famous southpaw chieftains included Alexander the Great, Julius Caesar, Tiberius, Charlemagne, Napoleon Bonaparte, Fidel Castro and even Joan of Arc and Queen Victoria of England. The bolt-action military rifles of the past, incidentally, were designed solely for right-handed infantry. Did these biased weapons make the left-handed, left-eyed, foot soldiers poorer snipers?

Left-handedness seems to dominate the contributors to two forms of the graphic arts: architecture and painting. Left-handed artists of the past have included Leonardo da Vinci, Michelangelo, Raphael, Albrecht Durer, Hans Holbein, M.C. Escher, and Paul Klee. The incidence of left-handedness amongst teachers in institutions of higher education and professional musicians is also significantly higher than in the general population [although none of the virtuoso violinists of the past century were lefties since the instrument is designed only for right-handed musicians. Yet some of the leading guitarists—also an instrument designed for right-handed musicians—were southpaws, including Paul Simon, Eric Gale and Albert King.]

Left-handed athletes have excelled in most sports except for professional boxing [although “Gentleman” Jim Corbett was a southpaw]. In addition there has been a conspicuous absence of great golfers who are left-handed. In tennis, however, being left-handed is sometimes considered an advantage over opponents who customarily play only against other right-handed players. Quite a number of the recent tennis champions have been southpaws [Connors, Laver, McEnroe, Vilas, Navratilova and Seles].

Are there other asymmetries regarding handedness? A recent study conducted by Christopher S. Roebuck, a professor of economics at Lafayette College in Pennsylvania concluded that “college-educated left-handed men earn almost 15% more, on average, than right-handed men with similar educations.” The study, a kind of left-handed vindication for the southpaws, made no mention of whether such an economic advantage pertained also to left-handed women.

More studies are clearly needed to determine the competitive status of the lefties in a biased world. Until then, these left-handed survivors must display a fragile bravado, celebrate a day of their own [August 13, International Lefthanders Day] and resort to valiant bumper stickers such as: “We are all born right-handed. Some of us, however, have overcome this handicap.”

— STANLEY M. ARONSON, MD

# Biohybrid Limbs: New Materials and New Properties

Roy K. Aaron, MD, and Jeffrey R. Morgan, PhD

**BIOHYBRID STRUCTURES ARE COMPOSED OF** both biological tissue and non-biological components. An example in current clinical use is the uncemented joint replacement, in which metal implants are integrated into bone. The resulting biocomposite, or biohybrid, has unique mechanical properties. In addition to orthopaedic endoprostheses (bone and joint replacements), current examples of successful biohybrids include growth factor augmented skeletal repair and engineered skin, cardiovascular grafts, and neuro-prosthetics. Other biohybrid structures in development include secretory cells embedded in implantable scaffolds, and a number of drug delivery systems and sensors.

The biohybrid limb is conceptualized as consisting of biological tissues and non-biological materials as endo- or exo- prostheses. Theoretically, a biohybrid limb can be constructed to improve function after traumatic tissue loss or therapeutic ablation. Conceptualizing a limb as a biohybrid organ frees the researcher and clinician from constraints imposed by the limitations of biological tissue or biomaterials, respectively. Biohybrid limb research integrates independent developments in regenerative medicine, neurotechnology, orthopedics, and robotic prostheses, to maximize limb function. The biohybrid vision includes optimized interfaces with, and control of, technologically advanced biomimetic prostheses.

Many of these concepts are expanded upon in the accompanying articles within this volume. Moreover, the following articles will illuminate an important aspect of biohybridity—these structures often possess new physical and physiological properties that require full understanding before they can be most effectively utilized in the clinical setting. Biophysical properties result from the interface between prosthetics and biological tissues. In the case of bone, a variety of textured or coated surfaces have been created to encourage bone to grow into and interdigitate with the prosthetic. These coatings create optimal porosity and can be supplemented by chemical adjuvants, such as hydroxyapatite. (Figure 1)

Here, we will present one example of a novel biohybrid structure—osseointegrated transcutaneous implants—that have the potential to create an improved interface between a residual limb after amputation and a biomimetic prosthetic limb.

Fixation of prostheses to residual limbs is currently achieved through plastic sockets that fit around the end of the limb. These devices are often uncomfortable, hot, and irritating to the skin—especially to traumatized and scarred skin. Moreover, scar and poor socket fit often lead to skin ulceration, infection and pain, all of which limit the use of prosthetic limbs. In fact, chronic pain, with or without skin breakdown, causes 25% - 35% of lower extremity amputees to abandon their prosthetic

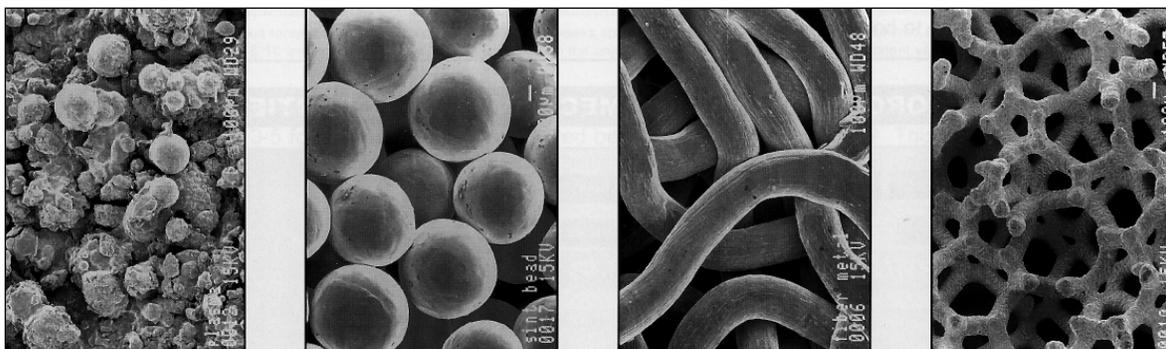
limbs and ambulation.

The technique of *osseointegration* is a promising method of fixing a prosthesis directly to bone, which has the potential to by-pass some of these problems. This technique integrates a titanium implant with bone, much like hip replacements; however, the implant extends from the bone to exit through the skin, creating an anchor for the prosthetic limb. (Figure 2) This method bypasses skin contact with the prosthesis, reducing pain.

In true osseointegration, the living bone becomes fused with the oxide layer of the titanium and this anchorage persists under normal conditions of weight bearing. This allows *osseo-perception*, i.e., the ability of patients with osseointegrated devices to identify tactile thresholds transmitted through their prostheses. Through increased osseo-perception, the biohybrid limb has the potential to improve amputee perception of his or her environment. Several fully internal osseointegrated devices have been described for orthopaedic applications, including metacarpal-phalangeal joints.<sup>1</sup> Indeed, titanium joint replacements in use worldwide incorporate osseointegration principles.

The application of these principles to amputees, however, has raised concerns because the titanium device is transcutaneous. Concerns have been raised not so much about the integration of the device with bone, but about the development of path-

**Figure 1: Scanning electron micrographs of textured or coated metallic implant surfaces**



Biophysical properties result from the interface between prosthetics and biological tissues. In the case of bone, a variety of textured or coated surfaces have been created to encourage bone to grow into and interdigitate with the prosthetic. These coatings create optimal porosity and can be supplemented by chemical adjuvants, such as hydroxyapatite. Each treatment creates different physical conditions, encouraging in-growth of soft or hard tissues.

*Image courtesy of J. Dennis Bobyn, Ph.D., Jo Miller Orthopaedic Research Laboratory, Montreal General Hospital, McGill University*

**Figure 2: Lower-limb prosthetic, fixed to the femur**



A transcutaneous titanium rod is affixed to the bone of the residual limb and protrudes from the skin. The exoprosthesis is attached to the protruding rod, bypassing contact with the skin.

ways around the implant through soft tissues where environmental contamination could cause titanium corrosion and bone infection. This could lead to further loss of bone, resulting in an even shorter residual limb, and thus even greater problems in affixing a prosthesis. Clinical reports on osseointegration are scanty and do not address questions of transcutaneous complications. However, anecdotal reports do describe infections and prosthesis loosening.

These complications may be due to a lack of soft tissue integration with the titanium implant, and the absence of a barrier between the internal and external environments. Percutaneous devices that penetrate the skin are widely used in a variety of other clinical applications, including peritoneal dialysis, indwelling catheters, and dental implants.<sup>1,2</sup> Each of these applications suffers from similar complications related to the effectiveness with which skin seals around the implant. Several distinct failure modes that limit long-term usefulness of these devices have been identified, including marsupialization, permigration, infection and abscess formation, and avulsion.<sup>3</sup> While it is true that the dermal response is critical for the at-

tachment of the skin and that it provides the bulk of the skin's mechanical attachment to the device, it is also well known that undesirable responses to percutaneous devices are common. Moreover, suboptimal attachment in the epidermis may influence events in the dermis. In recent years, it has become increasingly clear that cytokines and growth factors secreted from the epidermis, notably interleukin-1 (IL-1), influence cellular events in the dermis and vice versa. Significant quantities of IL-1 are released when keratinocytes are stretched.<sup>4</sup> Thus, suboptimal attachment of the epidermis may increase inflammation and affect the maturity of the connective tissue formed by the dermis. Concerns about infection and loosening, and consequent loss of bone in residual limbs, have focused our attention on the interface of soft tissue—particularly skin—with osseointegrated prosthetics. Our research goal is to develop an environmental seal by integrating skin and dermis with titanium, thus eliminating contact between the bone and the environment and restricting contamination of the prosthesis and bone.

Most osseointegration devices are made of titanium because of its strength, ductility, low density, and corrosion resistance.<sup>5,6</sup> The good corrosion resistance of titanium is the result of a strongly adherent oxide surface film.<sup>7,8,9</sup> The electrochemistry of titanium is such that, in the presence of oxygen, this film is rapidly repaired even if it is ruptured. However, hydrogen, because of its small atomic size, can penetrate the oxide, enter the titanium, and react with the metal to form hydrides which are very brittle, destroy the mechanical properties of the titanium and lead to materials fracture.<sup>7,8</sup>

Thus, conditions of low pH can lead to titanium failure. The most common mechanism of breakdown of the oxide film is crevice corrosion.<sup>5,6</sup> The metal may initially be covered with an oxide, but very slowly corrosion occurs and, as the metal is oxidized, the oxygen in the solution is consumed. These reactions can lead to the establishment of acidic conditions in the crevice, resulting in rapid corrosion of the metal. It is indeed well known that occluded biological solutions can be particularly corrosive because of the concentrations of inflammatory cells and their products, and the presence of acidic pH with high hydrogen content.

One way to avoid corrosion at the site of the implant is to locate cell growth directly onto the surface of the titanium. From the materials point of view, we are exploring two primary ways in which one could effect cell attachment—either by changing the composition and microstructure of the alloy, or by changing the morphology of the surface. To improve the soft tissue interface with osseointegrated prostheses, we are (1) determining the optimal surface chemistry and morphology of titanium for the attachment of epidermal keratinocytes and dermal fibroblasts, and (2) developing a finite element analysis model to understand the mechanics of the skin-prosthesis interface that will be used to improve device design.

One approach will be to treat the surface of the titanium in various ways in order to provide a porous surface that might enhance cell adhesion. One possible method is anodization of the titanium to produce a porous oxide, coating the surface with powder that could be sintered to different degrees of porosity. Another is the use of various mechanical surface-roughening treatments. We have devised a novel method to rapidly produce thin films of titanium and its alloys with which we can control the chemistry, grain size, and morphology of the metal surface. Experiments are underway to determine the stability of these surfaces under *in vitro* physiological conditions. We have also started initial testing of these surfaces and have set up quantitative fluorescent assays to measure cell number, cell adhesion, and cell morphology. These approaches will facilitate the rapid and quantitative screening of a large array of surface chemistries and morphologies to identify those optimal for cell attachment.

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## Regenerative Medicine for Limb Trauma

Roy K. Aaron, MD, Deborah McK. Giombor, PhD, Michael Lysaght, PhD, Edith Mathiowitz, PhD, and Michael G. Ehrlich, MD

### REGENERATIVE MEDICINE—THE ENGINEERING OF TISSUE OR ORGAN REPLACEMENTS—

is one solution to an entire spectrum of diseases, including the focus of our research, tissue loss following limb trauma and traumatic amputation.

### CELL BASED THERAPIES FOR TISSUE REGENERATION

Because many of the same signaling molecules that regulate cartilage development in embryogenesis are re-expressed in post-natal life during growth and repair, many investigators have taken a developmental approach to understanding and promoting cell growth and repair, in which connective tissue repair in post-natal life is studied as a recapitulation, at least in part, of early cell developmental pathways. In these early stages of development, competent cells are exposed to growth factors. In response, they can proliferate or differentiate, often creating complex tissues and organs.<sup>1</sup> This provides the theoretical basis for using growth factors to stimulate endogenous repair and to facilitate cell-mediated engineered repair.

Tissue regeneration involves the re-expression or re-induction of genes that regulate development.<sup>2,3</sup> Tissue engineering research will mostly likely require an increasingly complex understanding of the regulatory effects of endogenous physical and chemical gradients on progenitor cells and synthesis of extracellular matrix. Our observations have suggested a strat-

egy of introducing growth factors to repair bone or cell-based engineered constructs in order to stimulate proliferation and/or differentiation of progenitor cells. (Figure 1) While some success has been achieved by injecting single growth factors into skeletal defects, this strategy has been limited by problems of dosing related to pharmacokinetics that can result in loss of growth factors from the desired site by diffusion or inactivation, as well as an inability to sustain delivery.

### SYNOVIAL CELLS FOR CARTILAGE REGENERATION

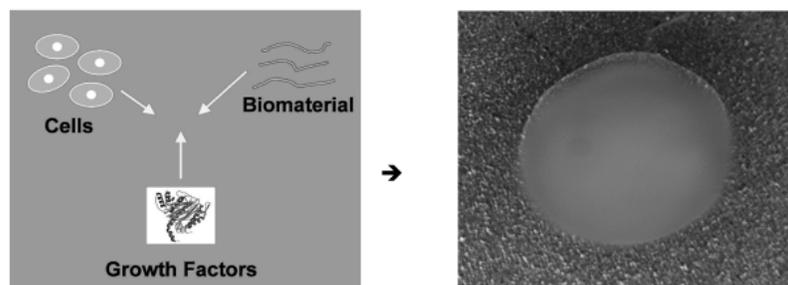
The membrane lining the synovial joint produces synovial fluid. It is particularly relevant to explore the tissue generating properties of synovial tissue because of its ready availability to the surgeon operating on joints. In addition, it has a dem-

onstrated propensity to undergo chondrogenesis.

Since synovium contains a mixed population of cells that respond differently to various growth factors, we first had to achieve isolation of separate synovial cell types with magnetic bead separation. Early in our research, we succeeded in isolating a progenitor cell population with strong predilection for chondrogenic differentiation. We then exposed this population to specific growth factors and signaling molecules involved in chondrogenesis: FGF-2, TGF- $\beta_1$ , and IGF-1. Each represents different classes of growth factors with documented effects on stem cells and chondrocytes. FGF-2 is a mitogen; TGF- $\beta_1$  stimulates differentiation; and IGF-1 promotes extracellular matrix secretion.

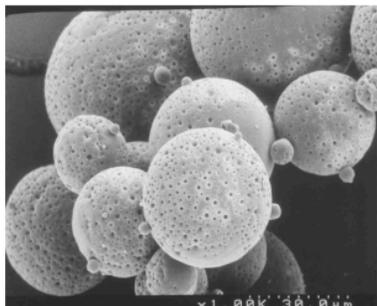
In order to maximize chondrogenesis, we studied high density synovial pellets in-

Figure 1: Fabricating a cartilage biocomposite



The cartilage biocomposite pictured above (right) has been fabricated from progenitor cells, growth factors, and a scaffold.

**Figure 2: Polymer beads**



Polymer beads are constructed from polylactic or polyglycolic acid and are biodegradable to CO<sub>2</sub> and water. Porosity can be controlled and, in turn, can regulate the release of growth factors.

cubated with FGF-2 and IGF-1, alone or in combination with TGF- $\beta_1$ . Our results suggest that (1) FGF-2 supplementation increased the cell number of synoviocytes; (2) TGF- $\beta_1$  stimulated chondrogenic differentiation in a dose-dependent manner; (3) IGF-1, combined with TGF- $\beta_1$ , can dramatically improve chondrogenesis compared to the supplementation of TGF- $\beta_1$  alone, and this improvement is both time- and dose- dependent. These results demonstrated, for the first time to our knowledge, the TGF- $\beta_1$ -dependent chondrogenic effect of IGF-1 and FGF-2 on synovial fibroblasts and the optimization of chondrogenesis by the sequential application of growth factors.

### POLYMER ENCAPSULATED DELIVERY OF GROWTH FACTORS FOR TISSUE ENGINEERING

Growth factors and cytokines are proteins involved in cell growth, repair and differentiation. One promising approach to the problem of growth factor delivery is encapsulation of growth factors in nano- or microspheres, which release cytokines over time.<sup>4</sup> In principle, several encapsulated growth factors could be delivered within physiological dosing conditions to a repair site, or included in cell-based engineered constructs in order to provide sequential or complementary release of growth factors that could act in a concerted fashion to optimize tissue repair. The kinetics of release may be either constant or cyclic over time, or triggered by an external physical force (e.g., ultrasound or pulsed electromagnetic fields).<sup>5,6</sup> Polymer microspheres have been fabricated in our laboratory in the size range of 0.1-10  $\mu$ m and have been used to encapsulate

and release a wide variety of bioactive molecules while maintaining greater than 90% bioactivity. (Figure 2) In particular they have been used to successfully encapsulate and release active growth factors and cytokines such as insulin, IL-2, IL-12, and growth hormone. To date, we have achieved encapsulation of FGF2 and TGF- $\beta_1$ . As part of our research in encapsulating TGF- $\beta_1$ , and release kinetics of TGF- $\beta_1$  are being determined.

We have also developed microsphere formulations that can deliver growth factors following a latency period. This facilitates the sequential application of growth factors, particularly IGF-1, that is important in cartilage regeneration. In particular, we have encapsulated IGF-1 in PLGA microspheres and showed active IGF-1 release over 80 days. By incorporating bovine serum albumin in the formulations, we were able to nearly eliminate the initial burst of IGF-1. (Figure 3a and 3b)

Furthermore, we created three-dimensional scaffolds from growth-factor-loaded microspheres using a unique vapor fusion technique. By controlling the

fusion parameters (i.e., time, amount of vapor, microsphere composition), we can create scaffolds of various shapes, sizes, and porosities that can release proteins under preprogrammed conditions. Such constructs may be useful for cell delivery in cartilage and other tissue engineering applications.

Immunoisolated cell therapy represents an alternative approach to delivery of growth factors and cytokines.<sup>7</sup> In this approach, cells that are genetically modified to constitutively release TGF- $\beta_1$  in both the active and latent form are encapsulated within a semi-permeable barrier (biodegradable polymer capsules) and implanted in a host. (Figure 4) Bioactive substances, e.g., TGF- $\beta_1$  or FGF2, then diffuse from the capsule. Using available techniques for creating capsules and measuring and controlling their performance, *in vitro* release profiles from microencapsulated genetically modified living cells have been measured and optimized. NIH 3T3 murine fibroblasts have been genetically modified to synthesize and secrete human TGF- $\beta_1$  and have been encapsulated in microspheres. The approach is highly appealing because released growth factors are freshly produced and biologically active. Moreover, release rates are constant in time without the detrimental “starburst” effect.

Our group has also developed and characterized *in vitro* and *in vivo* a family of microcapsule delivery vehicles comprising Ca<sup>2+</sup>-alginate-coated fibroblasts genetically modified to constitutively release TGF- $\beta_1$ . No evidence of adverse host reaction was identified. Overall, the data suggests that these novel capsules are suitable for evaluation as sources of TGF- $\beta_1$  in applications such as bioartificial cartilage.

**Figure 3: IGF-1 Release**

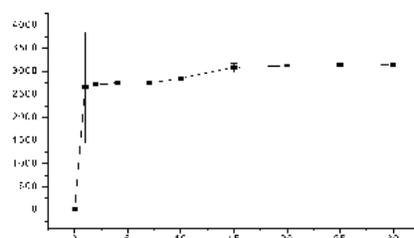


Fig. 3a: Release of IGF-1: Standard Microsphere

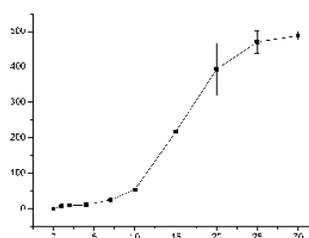
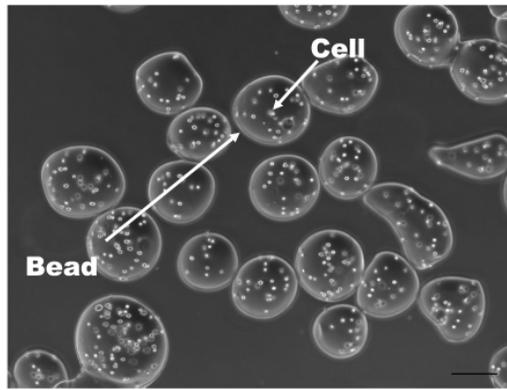


Fig. 3b: Delayed Release IGF-1 demonstrating that the growth factor does not appear until day 10 of culture.

**Figure 4: Cells encapsulated in polymer beads**



Cells are immobilized within polymer microcapsules. Cells can be transfected with one of several genes to function as producers of proteins such as growth factors.

### **TISSUE ENGINEERING SOLUTIONS FOR BONE LENGTHENING**

A serious problem for amputees is short residual limbs, which are particularly common after traumatic amputations. When the residual limb is too short, a higher functional amputation level is required for prosthesis use. For example, short residual proximal tibias may not allow fitting with a below-knee prosthesis and may require extension of the prosthesis to the thigh, forcing the user to function as an above-knee amputee. Similar problems exist in the upper extremity for both above-elbow and below-elbow prostheses. Often, the higher functional amputation requires a heavier, and thus more awkward, proximal prostheses, which in turn increases the energy cost of movement. Proximal transfemoral amputations can adversely affect sitting balance and may require functional hip disarticulation prostheses.

One strategy is to lengthen the short residual limb (without bone grafting) by producing new bone between vascular bone surfaces created by an osteotomy and separated by gradual distraction.<sup>8</sup> (Figure 5) This process is called *distraction osteogenesis*. A related operation, *bone transport*, refers to the movement of a segment of bone within the limb. A major benefit of limb lengthening with distraction osteogenesis and bone transport is that these techniques can convert a proximal level of amputation to a more distal one. Bone transport techniques have been used to convert the level of amputation, in one case, from hip disarticulation to above-knee, with gain in length of 9 cm.<sup>9</sup>

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## **Tissue engineering strategies hold the promise of accelerating the rate of elongation, maximizing the length of regenerated bone, and diminishing osteoporosis and refracture.**

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Limb lengthening with external fixation is not new. These methods have been used to generate bone to bridge intercalary bone defects, correct deformities, and treat bone loss secondary to tumor, infection, and trauma. The first reports of bone lengthening for purposes of lengthening the limb were reported in the early 1900s. The rate of lengthening is critical both to ensure bone healing and to minimize soft tissue complications, including skin necrosis and neuropraxia. Techniques used to accomplish distraction osteogenesis include external fixation with monolateral half-pin frames, ring external fixation with wires under tension (Ilizarov technique), and lengthening over intramedullary nails. Good results have been obtained with all techniques; choosing among them often depends upon the extent of angulatory or rotary deformities.

Stability of the fixation construct is critical since unstable constructs can lead to premature consolidation or nonunion. Other problems that have been encountered are long consolidation times, pin infections, inadequate skin coverage, and joint stiffness. Issues that may be related to these complications, and that therefore may permit reduction in their frequency, are vascularity and tissue oxygenation, nutritional status, and immunocompromise.

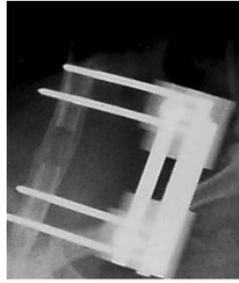
Tissue engineering strategies hold the promise of accelerating the rate of elongation, maximizing the length of regenerated bone, and diminishing osteoporosis and refracture. Some of these techniques include the use of biomimetic scaffolds, growth factors, demineralized bone matrix, gene therapy, and interaction with physical stimuli, including mechanical, ultrasound, and electrical.

While the biology of distraction osteogenesis has been fairly well explored, no paradigm exists for augmented distraction. Therefore we are examining the effects of growth factors and physical stimuli on vascularization and the synthesis of cartilage and bone extracellular matrix using biological, radiographic, and biomechanical measurements of consolidation with a number of lengthening rates.

One complication that can directly affect rehabilitation and the restoration of limb function is delayed bone union after lengthening. Our investigations have thus focused on augmenting consolidation. One method for optimizing consolidation and healing of the lengthened segment involves progressive weight-bearing. Our studies have collectively demonstrated that matrix formation and calcification occurred earlier in animals with distraction osteogenesis that were permitted graded weight-bearing, compared to non-weight-bearing animals.<sup>10,11</sup> Weight bearing has also been shown to stimulate new blood vessel formation during distraction osteogenesis. This suggests that early regenerate bone is augmented by mechanical loading and supports the concept of early weight-bearing after limb lengthening.

Another potentially effective approach to optimizing bone consolidation involves low intensity ultrasound stimulation.<sup>12</sup> Radiographically, healing of the ultrasound-treated bones preceded that of the control by approximately one week. The bone volume fraction was significantly higher in the

**Figure 5: Limb-lengthening**



**Fig. 5:** The gap of lengthened bone with reconstitution of the periosteum and early calcification.

ultrasound-treated animals. The ultrasound-treated femurs were 20% stiffer and 33% stronger than the control femurs.

Bioactive peptides can be used to stimulate healing after distraction osteogenesis. **Platelet-derived growth factor (PDGF)** was discovered in 1974, following the observation that material released from platelets during clotting was capable of promoting the growth of various types of cells. PDGF was subsequently purified from platelets, but it is now known to be produced by a number of cell types, and it has also been found to be a mitogen for almost all mesenchymally derived cells (blood, muscle, bone/cartilage, and connective tissue).

To date, we have manufactured new *fixators* for distraction in the rat (i.e., surgical units that hold the bone in a fixed position after the surgery to separate the two ends of the bone being lengthened). We have also developed instruments to position and tighten these fixators. In addition, we have developed a collagen formulation that would gel almost immediately upon hitting body temperature, which would prevent the PDGF from flowing out from the interstices of the minimally distracted bone. Moreover, we have begun developing a bioassay to evaluate the activity of the released PDGF from our collagen gel utilizing the mitotic effect on fibroblasts. Some of our preliminary work using multiple injections looks promising in terms of early healing.

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# Biomimetic Prostheses: The Next Generation

Hugh Herr, PhD, and Samuel Au, MS

**PERHAPS THE MOST TANGIBLE COMPONENTS** of biohybrid limb research are advances in lower extremity prosthetic systems. These systems will employ biomimetic control, muscle-like actuation, and neuro-sensors that will let leg amputees experience improved responsiveness to their actions and wishes. The goal of this research is to restore amputee limb function to near normal levels. Specifically, we are achieving improvement in gait stability and speed, and metabolic economy of gait.

This research focuses on two lower extremity systems: a variable-damper knee prosthesis, and a motorized ankle prosthesis. Unlike most current, passive prostheses, these systems will simulate the dynamics of joint impedance\*. In addition, the system will contain mechanical power generation to better simulate the natural dynamics of walking.

## BACKGROUND

In the 1970s, Professor Woodie Flowers at MIT conducted research to develop the prosthetic knee joint from a passive, non-adaptive mechanism to an active device with variable damping capabilities.<sup>1-4</sup> Using the Flowers' knee, the amputee experienced a wide range of knee damping values throughout a single walking step. During ground contact, high knee damping inhibited knee buckling, and variable damping throughout the swing phase allowed the prosthesis to swing freely before smoothly decelerating just prior to heel strike. While the Flowers' knee was never sold commercially, several prosthetic companies manufactured similar variable-damper knee products.<sup>5</sup> Actively controlled knee dampers offer advantages over mechanically passive knee systems. Most notably, amputees can change gait speed and descend inclines/stairs with greater ease and stability.<sup>6-8</sup> Typically, ankle-foot systems comprise elastomer\* bumper springs or carbon composite leaf springs (Figure 2) that store and release energy throughout each walking or running step.<sup>5</sup> Lower limb prosthetics, however, still do not restore enough limb function. In order to mimic the behavior of the human ankle

and to increase gait symmetry and walking economy, a prosthetic ankle-foot device should actively control joint impedance, motive power, and joint position.

## PROBLEMS ASSOCIATED WITH LOWER-EXTREMITY PROSTHESES

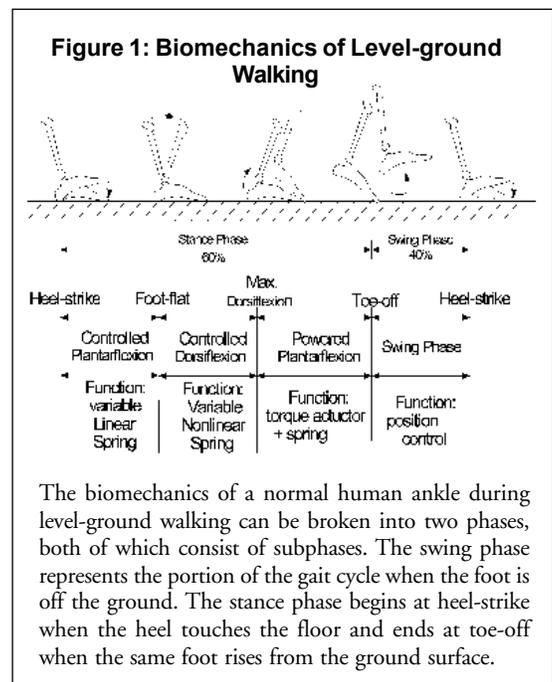
Commercially available lower-extremity prosthetic devices do not vary spring stiffness or motive force like natural limbs. Nor do they mimic the limbs' natural energy storage and return systems. This causes many problems for leg amputees. Recent studies suggest that amputee balance, especially when walking over rough surfaces, may improve if the stiffness of the prosthetic ankle is adjusted in response to changes in ground stiffness. In addition, amputees using a powered knee prosthesis can walk at a faster pace and with an improved metabolic economy compared to those with conventional knees, which only dissipate mechanical energy.

The local mechanical sensors employed in today's variable-damper knee prostheses are another limitation for the leg amputee. Without direct input from the user to indicate intention, available prostheses cannot determine whether a patient wishes to turn to the right or to the left, or whether an obstacle falls directly in the amputee's intended pathway. Since passive prosthetics place high metabolic demands on the body's ambulation systems, amputees also typically experience undue fatigue.<sup>9-11</sup> In short, although some improvements have been observed with variable-damper knee designs, problems still remain.<sup>11</sup>

## BIOMIMETIC ANKLE-FOOT PROSTHESIS DESIGN

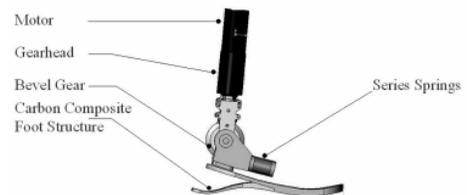
Since the goal is to produce a prosthetic that approximates a normal gait, research into the function of the human ankle during level-ground walking was necessary to provide the design specifications for the ankle-foot prosthetic system.

The gait cycle begins with the heel strike of one foot and ending at the next heel strike of the same foot. The main subdivisions of the gait cycle are the stance



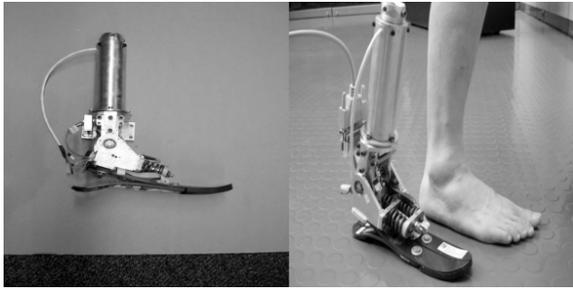
The biomechanics of a normal human ankle during level-ground walking can be broken into two phases, both of which consist of subphases. The swing phase represents the portion of the gait cycle when the foot is off the ground. The stance phase begins at heel-strike when the heel touches the floor and ends at toe-off when the same foot rises from the ground surface.

## Figure 2: Mechanical Design of the Human Ankle-foot Prosthesis



There are four main mechanical elements in the human ankle-foot prosthesis: (a) a high power output motor (Maxxon RE-max 40), (b) transmission (gearhead and the bevel gears), (c) series springs, and (d) a carbon composite leaf spring prosthetic foot. We combine the first three components into a rotary Series Elastic Actuator (SEA) to mimic the behavior of the human ankle joint, while the elastic leaf spring mimics the function of a human foot.

**Figure 3: Prototype ankle-foot prosthesis**



A photograph of the biomimetic ankle-foot prosthesis prototype (left) and a SolidWorks model next to a human foot (right).

phase and the swing phase. The stance phase begins at heel-strike when the heel touches the floor, and ends at toe-off, when the same foot rises from the ground surface. Stance phase can be subdivided into three sub-phases: controlled plantar flexion, controlled dorsiflexion, and powered plantar flexion. The swing phase represents the portion of the gait cycle when the foot is off the ground.

Research into gait mechanics allowed researchers to design an ankle-foot prosthesis that mimics the biomechanics of a normal limb during walking. We developed a finite state machine\* to implement the basic control system for the prosthesis. As in normal walking, the prosthesis was controlled as a linear torsional spring with stiffness  $K_{CP}$  in controlled plantar flexion. (Figure 1) In controlled dorsiflexion, we simply used two linear springs to approximate the nonlinear spring behavior of the human ankle. In the design

process, several criteria for biomimetic function were established. Much like a natural ankle, the biomimetic ankle was modeled as a torque source in series with the controlled dorsiflexion spring, and additional amounts of energy can be added to the ankle joint during powered plantar flexion. In addition, the prosthetic ankle must be capable of changing its stiffness within each phase of gait; and it must be capable of controlling joint position during the swing phase.

## Commercially available lower-extremity prosthetic devices do not vary spring stiffness or motive force like natural limbs.

There are four main mechanical elements in the system we designed to provide these capacities: (a) a high power output motor, (b) transmission (gear head and the bevel gears), (c) series springs, and (d) a carbon composite leaf spring prosthetic foot. The first three components are termed a rotary **Series Elastic Actuator (SEA)** and mimic the behavior of the human ankle joint, while the elastic leaf spring mimics the function of a human foot. (Figure 2)

A Series Elastic Actuator has been previously developed for legged robots. It consists of a dc motor in series with a spring (or spring structure) via a mechanical transmission. The SEA provides

### GLOSSARY

- Joint impedance:* The stiffness and damping of a joint
- Elastomer:* Any of various elastic substances resembling rubber
- Finite State Machine:* A programming structure comprising distinct states and transitional conditions between states

precise force control by controlling the extent to which the series spring is compressed. An SEA has several biomechanical features that make it a good choice for human rehabilitation applications. SEAs are force controllable actuators; they are safer to use with human subjects than direct drive systems because a limiting maximum force can be specified that will not cause harm to the human user. A prototype of the actual prosthesis is shown in Figure 3. The specifications of the prosthetic system are listed in Table 1.

Because we believe that the amputee's device acceptance and comfort should be criteria for selecting certain adjustable values—such as spring stiffness and the amount of power generated during specific phases of the walking gait—in our initial pilot investigations, we felt it was reasonable to allow the subject to select these parameters based on his/her own walking preferences. To achieve this goal, we developed a graphical user-interface that allows the amputee to adjust the settings and timing of these values.

In our pilot study, the subject selected a stiffness value that eventually converged to the normalized biological value we had established during our study of the biomechanics of the walking gait. Participant comments confirmed that the virtual spring improved shock absorption during heel-strike and also allowed for a smoother transition from Controlled Plantar Flexion to Controlled Dorsiflexion. During its use, we observed that the prosthesis behaved more naturally than a conventional passive prosthesis and allows for a more natural gait.

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	Current Design	A 75kg person
Peak Power	440W	240W
Peak Torque	340 Nm	127.5Nm
Peak Velocity	25 Nm at 5 rad/sec	19 Nm at 5 rad/sec
Weight	2.5kg	N/A
Height	0.32m	N/A
Max. Allowable Dorsiflexion	25 deg	25 deg
Max. Allowable Plantar Flexion	45 deg	45 deg

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## Neuromotor Prosthesis Development

*John P. Donoghue, PhD, Leigh R. Hochberg, MD, PhD, Arto V. Nurmikko, PhD, Michael J. Black, PhD, John D. Simeral, PhD, and Gerhard Friehs, MD*

**UNLIKE HUMAN LIMBS, TRADITIONAL, PASSIVE PROSTHESES** have practically no ability to respond to anything but the most basic aspects of our movement intentions. In addition, traditional prostheses cannot communicate sensory information to the brain. Biohybrid limb research seeks to restore sensory and motor signals meant for natural limb function by creating an interface that provides two-way communication between the prosthetic limb and the nervous system. The goal of our research is to create a biohybrid interface that communicates directly with the nervous system.

### NEUROMOTOR PROSTHESES (NMPs)

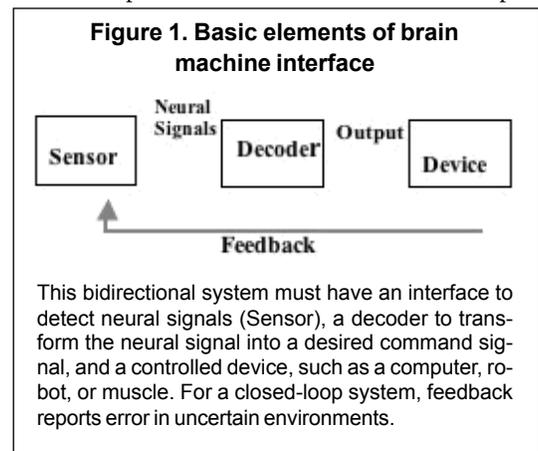
In the human nervous system, sensory and motor information are represented in patterns of electrical impulses (neuronal action potentials), often called spikes. Research into these patterns has paved the way for the development of closed-loop neuromotor prostheses (NMPs), which have the potential to enable bidirectional interaction between the human nervous system and external devices. In the case of semiautonomous robots, such devices could be independent of the human body, but capable of communicating with and being controlled by human users. In the case of

biohybrid limb prostheses, the devices themselves could replace limbs lost secondary to traumatic amputation, vascular or medical disease, and the ideal prosthesis would mimic both natural motion and sensation.

The emerging technology of NMPs combines cutting-edge biomedicine, neuroscience, mathematics, computer science, and engineering. This type of interface transcends earlier controllers because it is based on neural spiking, a source of information-rich, rapid, complex control signals from the nervous system. NMPs promise an entirely new paradigm for building bionic systems that can restore lost neurological functions.

For example, our team, together with a Brown spin-off company, *Cyberkinetics Neurotechnology Systems, Inc. (CKI)*, has already created a system that records human brain signals, decodes them, and transforms them into movement commands. The system consists of a match head sized platform with 100 thread-thin electrodes that penetrate just into the surface of the motor cortex where commands to move the hand

emanate. The pattern of complex neural signals is decoded by a rack of computers that displays the resultant output as the motion of a cursor on a computer monitor—as if the thoughts to move the hand had moved a computer mouse. This neural command signal has been used by persons with tetraplegia to control a computer for spelling<sup>1</sup>, to run software, or to use assistive devices that control a television.<sup>2</sup> While computer cursor motion represents a form of virtual device control, this same command signal could be routed to any of a number of devices to command motion of paralyzed muscles or the actions of prosthetic limbs; indeed, simple robotic arm control has already been achieved in pilot studies<sup>2</sup> and we have achieved pre-



liminary control of an electric wheelchair.<sup>1</sup> Joining expertise in human functional neurosurgery and neurology (Friebs and Hochberg), computer science and robotics (Black), neuroscience (Donoghue), and engineering (Nurmikko), this team has already completed initial work on potentially commercial elements of first-generation NMP technology now being developed through CKI.

To make further progress towards a useful product, the current pilot system must become miniaturized, wireless and fully implantable. Our team is developing these key elements of advanced NMP technology: integrated microscale signal processors, innovative broadband optical telemetry and powering, and miniaturized processors are all in development. Reliable signal control is also essential for day-to-day use. We are working on new mathematical models to transform a small sample of human neural recordings into a rich and useful control signal. In addition, we are working to create an interface that can provide sensation via low levels of patterned electrical stimulation to the sensory areas of the brain. In this way we hope to provide an NMP that creates two-way communication between machines and the nervous system.

## RESEARCH AND TRANSLATIONAL GOALS

This research provides the foundation for a system that could ultimately allow paralyzed people a greater degree

of independence, communication and mobility if they were able to control – simply through their own movement intentions – computer, robotic, or prosthetic interfaces. Long-term goals include a new class of devices necessary for human NMPs to operate more effectively, and to elucidate the principles of their operation. Intermediate goals include the development of both control algorithms and user interfaces that would enable human neural control of robot navigation tasks or other complex interactions.

## Modeling the Brain Computer Interface

The initial technology of Brain Computer Interfaces (Figure 1), of which NMPs are one type, consists of three key components: a neural interface, a decoding system, and a user interface (effector); a closed-loop system would be completed by a feedback signal from the effector to the brain. Feedback would be achieved by very low level electrical impulse sequences that attempt to activate a neural apparatus that participates in sensation. Core elements of the current research include:

1. An optimally designed and extensively tested microelectrode array. Microelectrode array fabrication incorporates controlled design and manufacturing of a one-hundred electrode sensor, a compact 4 x 4

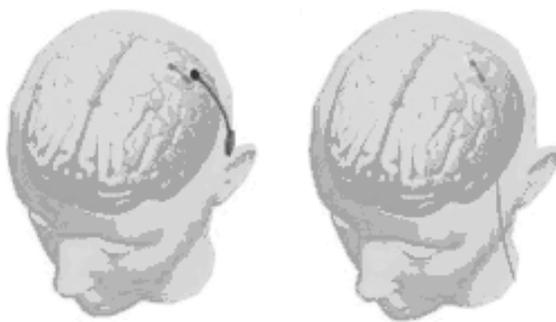
mm device that communicates with external electronics via an ~ 13 cm cable and a percutaneous Ti pedestal. Long-term pre-clinical studies in Dr. Donoghue's laboratory showed that the array is sufficiently stable to provide long-term recording of neuronal spikes suitable for NMP use.<sup>3</sup> The implant testing and design was submitted to the FDA for a proposed pilot clinical trial in 2004.

2. Signal acquisition and processing by specialized microelectronic device technology. A complete system is produced by Cyberkinetics, and miniaturized versions are being developed by our group to make the devices fully implantable, automated and portable.
3. Decoding based upon a principled mathematical framework has been developed by Drs. Black and Donoghue and their colleagues. Decoding efforts attempt to extract the maximum amount of information related to movement intentions from the sample of neurons detected using the implant. The signal is used for real-time control. Computational methods for signal processing are used to improve the quality of control. These methods attempt to achieve the speed and accuracy of an able-bodied human using a computer mouse to operate a standard PC.
4. Implementation of decoded signals as a control source. Once a brain derived control signal has been created, it can be used to operate a wide range of devices that improve independence, mobility and communication for those with limited movement abilities. Control signals can be used to run a computer and assistive technologies. In addition, control signals have been used to direct robotic arms. The signals are also potentially useful to reanimate limbs by driving electrical stimulators in paralyzed but otherwise operational muscles or actuators in advanced prosthetic limbs.

## DECODING THE HUMAN BRAIN

Decoding is the task of transforming complex neural patterns into a meaningful control signal that can drive physical or biological devices. This involves two key parts: First, we must understand how the brain adapts to control new devices and how we can best train the brain to control a new motor system. Second, we must mathematically model the way neural signals encode information about movement, and then exploit these models to develop a real-time "translator" between the neural signals and the inputs needed to control new devices.

**Figure 2. Implantable cortical microsystem overview**



Microsystem with an active implantable unit in soft encapsulation; transdermal IR telemetry; inductively or IR coupled powered delivery clock

Implantable microsystem connected to subcutaneous high speed fiber optic link; IR power delivery and telemetry through subcutaneous fiber coupled to abdominal/chest cavity unit.

This illustrates two adaptations of the same basic microsystem design for high-fidelity transcutaneous neural signal extraction at high data rates.

We have made substantial progress in this task. Using mathematical algorithms, we can convert motor cortex spiking activity into a continuous reconstruction of hand position, and classify patterns of motor cortex activity into discrete choices.<sup>4,7</sup> Recently we have developed “multi-state” methods that enable the decoding of continuous cursor trajectories and discrete “click” activities from the same population of cells.<sup>8</sup> Unique to this endeavor is the need to develop training methods parallel to new decoding algorithms; in designing algorithms one must take into account how the brain learns and how best to train it.

Accurate decoding can create a richer repertoire than current, fairly simple, scenarios in which the decoding of hand motion is either in one of a fixed number of directions or is a continuous reconstruction of two-dimensional hand trajectory. Our principled mathematical approach provides the foundation to enable the control of physical devices such as wheelchairs, prosthetic arms and dexterous robot hands. In particular, tasks such as manipulating, grasping, pushing, and gesturing involve the composition of more primitive motions. For example, even a simple action such as picking up a block may be composed of a preparation phase, a ballistic hand transport motion, manipulator positioning using visual servoing, and, finally, a grasping motion. Ultimately, the challenge is to develop a prosthetic device under neural control that is capable of executing all such compositional actions. Achieving this high-dimensional control will require basic scientific and engineering advances to determine the full extent of information available from neural spike trains.

Challenges remain, however. For example, decoders in use day to day by patients will need to function adaptively to deal with changes in the system that can arise from instabilities in the sensors or in the biological system. In addition, available neurons may change over time as sensors move even slightly in the tissue. For development purposes, we simulate more complex actions on a computer screen, where we can readily control the properties of a wide range of devices. This knowledge will set the stage for the development of actual devices that can serve real world interactions,

such as navigation in complex environments or control of multidimensional manipulators requiring dexterous finger, hand, and arm movements of an artificial device.

## **RESEARCH TOWARDS WIRELESS FULLY IMPLANTABLE NEURAL INTERFACES**

The overall goal of this project is to develop a fully implantable wireless multi-neuron sensor for broad research, neural prosthetic, and human neurodiagnostic applications. The implantable microsystem is based on the sensor electrode platform which has been extensively evaluated in preclinical animal studies, and now in four tetraplegic humans who are part of Cyberkinetics’ BrainGate pilot clinical trials. Related work aims to achieve multi-site stimulation to serve as an input interface for human and animal research applications.

The miniaturized brain implantable NMP microsystem-on-chip now under development at Brown has unique design features; it is flexible and scalable to allow transmission of increasingly larger amounts of neural information from the cortex to assistive technologies. The microsystem design architecture is also compatible with the longer term prospects of connecting the motor cortex to muscle nerves *intra-corporis* via a fiber optical network within the body, as well as via external prosthetic devices. In the development of the new NMP technology, we will be guided by experience gained from ongoing BrainGate human trials that employ passive microelectrode recording arrays, which are coupled by a percutaneous connector to external electronic modules.

Early prototypes of the implantable microsystems are under way, which incorporate advanced ultra-low power microelectronic circuits and processors with optoelectronic devices as integrated cortical implants, shown schematically in broad overview in Figure 2. This project charts a new pathway to human neuroprosthetics, well beyond the current state-of-the-art, while ultimately endeavoring to create a platform for a new neuro-technology paradigm for “whole-body” prosthetic networking via cortical interfaces. The design of the new implantable NMP microsystems will lever-

age information acquired from human clinical trials, including the experience gained with the present external cabling system developed by Cyberkinetics. The goal of the microsystem-on-chip is to enable very high data rate wireless transmission of high fidelity neural signals (spikes and LFPs) with transcutaneous powering and signal transmission. We have already achieved an initial prototype 16-channel microsystem which has been tested at the benchtop and initial rat animal studies.

## **CONCLUSIONS**

As they apply to biohybrid limb research, on-going advances in neural interfaces, microelectronic devices and decoding may allow dynamic linkages between the cortex and robotic prostheses through novel systems, such as the NMP system we are developing. Ultimately, these technologies could provide direct brain control of artificial limbs for amputees, or direct control of muscles for those with paralysis, as well as an entirely new means for physical monitoring and repair of the human nervous system.

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# Identifying Clinically Meaningful Improvement In Rehabilitation of Lower-Limb Amputees

Linda Resnik, PhD, PT, OCS

**THE EFFECTIVENESS OF TISSUE ENGINEERING,** and both surgical and prosthetic interventions for lower limb amputees must be assessed rigorously through carefully designed outcome studies. While objective measurements such as faster gait speed and better balance are important ways of evaluating rehabilitation success, they are insufficient without an assessment of the patient's subjective experience of intervention effectiveness. Thus, the outcomes that we use to evaluate our interventions will include physical performance measures as well as measures of the amputee's subjective experience of prosthetic satisfaction, quality of life, and mobility.

For small groups of subjects, the choice of highly reliable and responsive outcomes measures is imperative. The best instruments for use with individual patients and small group studies have superior measurement properties: in particular, reliability, measurement range, and responsiveness. However, not all measurements work with individuals or small groups. Scales with large floor or ceiling effects, or substantial numbers of patients scoring at the bottom or top of the scale, for example, are not appropriate choices for measuring individual-level

change. In addition, some instruments may lack the psychometric properties that detect change on the individual level.<sup>1</sup> To assess the effectiveness of interventions in clinical practice and small studies, measures must be responsive to change on an individual level, and research on responsiveness must assist in interpretation of scores.

**In the ceiling effect, there is little room for patients to show improvement, because they already score at the high end of the scale.**

In large clinical trials, the effectiveness of interventions is assessed statistically, by comparing mean change in outcomes scores between groups of patients. These same comparisons are impossible in clinical practice or trials using very small samples. Thus, common measures of responsiveness—such as effect size,<sup>2</sup> stan-

dardized response means,<sup>3</sup> or the responsiveness statistic<sup>4</sup>—summarize test responsiveness and are useful for making relative comparisons between measures, but do not contribute to the interpretation of test results in individual subjects or patients.<sup>5</sup> For interpretability at the individual level, one should be able to answer questions such as, “Does a change in score of 10 points in a certain measure denote an important change for these patients?” and “Is a 5-point change in score the same as a 10-point change in score?”

Data on two properties, **minimum detectable change (MDC)**<sup>6-8</sup> and **minimal clinically important difference (MCID)**<sup>9,10</sup> can assist in interpreting scores for individuals and small groups of patients. Minimum detectable change is a statistical measure of meaningful change, defined as the minimum amount of change that exceeds measurement error.<sup>8</sup> From a statistical perspective, an individual patient is considered to have changed only when the difference between the previous score and the current score exceeds the MDC associated with the measurement.<sup>7</sup> MCIDs, on the other hand, define the threshold at which an individual has experienced a clinically relevant change.<sup>9,10</sup>

The goal of my current research is to create more appropriate and productive outcome measures for lower limb amputees using recent advances in the selection and interpretation of assessment measures, specifically in the areas of responsiveness, sensitivity to change, and the interpretability of measurement change scores. Because this study is designed to integrate patient self-reports with performance-based measures of limb function, this study covers a range of both types of assessment measures. This will be a multi-site study with repeated measurements of subjects. Data will be collected at five sites (the Providence, Boston, and Miami VA Medical Centers, and two other non-VA hospitals). The tests are being administered by physical therapists observing and grading physical performance of activities.

## MEASURING DETECTABLE CHANGE

In order to be responsive to change, measurement instruments must detect change when it has occurred, and remain stable when change has not occurred. The ability of an instrument to detect relevant clinical change as judged by an external criterion, a type of construct validity, is considered by some to be the most important measurement property for evaluating a scale's usefulness in making individual patient decisions.<sup>11</sup>

Prior research suggests that there may not be a single MCID value that is applicable across all patients because the MCID of instruments can vary depending on the patient's baseline state and the methodology used to calculate it.<sup>7</sup> Thus, we are using several methods to calculate the MCID within self-report

measures. Our first method, modeled after that used by Jaeschke<sup>9</sup> and Juniper<sup>12</sup>, will calculate the mean change in subscale score that corresponds to changes in external criteria. Our second method, modeled after Stratford,<sup>11</sup> Riddle,<sup>13</sup> and Bruynesteyn,<sup>14</sup> will employ diagnostic test methodology and use information from stable and changed patients. In this method, the MCID of each self-report instrument subscale will be compared by developing receiver operating characteristic (ROC) curves.

In both methods, external criteria (anchors) will be used to identify patients who have changed by a clinically meaningful amount. We expect that the use of these two methods and variety of external criteria will yield variability in MCID calculations, allowing us to obtain a range of MCID parameters that can be useful for interpretability of score change.

At the end of our analyses we will have accumulated data on MDC as well as MCID calculated by ROC and mean score change method. We will aggregate the evidence from these analyses to make recommendations on the proper interpretation of change scores for each measure. Several authors have highlighted the merits of triangulating both distribution and anchor based approaches to define meaningful changes.<sup>15-18</sup> Using triangulation, we will also be able to make recommendations about those self-report instruments that are the most sensitive and responsive to change.

## CORRECTING FOR FLOOR AND CEILING EFFECTS

Another problem in current outcome instruments is the inability to measure change for patients who fall outside ranges of test expectation. These "floor and ceiling" effects occur when an instrument lacks sufficient scale range, resulting in a large proportion of scores at the very top or bottom of the range. In the ceiling effect, there is little room for patients to show improvement, because they already score at the high end of the scale. For example, an amputee patient who is able to run, but is limited to short distances, might score off the charts, despite self-reported frustration with the undue fatigue caused by higher rates of metabolic stress related to prosthetic use.

**Table 1: Physical Performance and Self-Report Assessment Measures Undergoing Analysis**

### PHYSICAL PERFORMANCE MEASURES

#### Timed walk tests

Two and six minute timed walking tests are designed to assess mobility, and or cardiovascular fitness. The distance covered in the allotted time is taken as the measurement of performance.

#### Timed Up and GO (TUG)

The TUG is a brief performance based measure of basic mobility that incorporates walking and turning while walking, balance and transfers.

#### Amputee Mobility Predictor (AMP)

The amputee mobility predictor is an instrument designed to measure ambulatory potential of lower-limb amputees both. The AMP consists of twenty one items that evaluate ability in transfers, sitting and standing balance as well as gait skills.

### SELF-REPORT MEASURES

#### SF-36

SF-36 is a generic instrument containing 8 different scales measuring physical and mental health constructs. Three of the SF-36 scales will be tested, General Health, Physical Function, and Role Physical.

#### PEQ

The Prosthetic Evaluation Questionnaire (PEQ), is a condition specific instrument developed for prosthetic users. We will test four of the PEQ's nine scales: General Health, Mobility, Transfers and Prosthetic Utility

#### OPUS

The Orthotics and Prosthetics Users Survey (OPUS) is a condition specific instrument that measures outcomes pertinent to prosthetic as well as orthotic users.<sup>6</sup> Three of the OPUS's four scales will be tested Lower limb functional measure, Health Related Quality of Life scale, and the Follow-up Evaluation of Satisfaction with Device scale.

#### Patient Specific Functional Scale (PSFS)

In the PSFS, the patient is asked to select up to five main activities that he or she finds difficult to do because of the amputation. Then the patient is asked to provide a rating of his or her current ability to complete these activities.

One aim of this study is to identify scales with large floor or ceiling effects, which are inappropriate choices for measuring individual-level change. We will assess the extent of floor and ceiling effects using two methods. First, we will examine the distribution of scores for each scale, observing the shape and presence of score clustering. Scores clustered at the low end of the scale suggest the presence of floor effect, whereas scores clustered at the high end of the scale would suggest presence of a ceiling effect. Next, we will calculate the minimum and maximum scale scores around which the MDC could be placed while maintaining the score above the bottom (floor) and below the top (ceiling) and then calculate the percentage of the sample achieving scores that range within the MDC of the lowest (floor effect) and highest (ceiling effect) for each subscale. Scales with large floor or ceiling effects would not be appropriate choices for measuring individual-level change and will not be included in our future testing.

## STUDY MEASURES

Two types of measurement instruments will be tested in this study: self-report measures of health-related quality of life (HRQL) and performance-based measures of mobility. Self-report HRQL instruments use patient questionnaire responses to measure multiple domains of health that include physical, psychological, emotional, and social dimensions.<sup>19</sup> The self-report instruments include the Prosthetic Evaluation Questionnaire (PEQ),<sup>20</sup> the SF-36,<sup>21</sup> the Orthotics and Prosthetics Users' Survey (OPUS),<sup>22</sup> and the Patient-Specific Functional Scale (PSFS).<sup>23</sup> The performance measures chosen for this study are the two- and six-minute walk tests,<sup>24</sup> the Timed Up and Go (TUG) and the Amputee Mobility Predictor.<sup>25</sup> Each instrument is described below. (Table 1)

We will use global transition ratings as an external criteria for change in self-report measures. Three separate transitional scales will be used, one for general health, one for prosthetic satisfaction, and one for physical function. We will classify subjects as having either changed or remained stable by asking if there has been any change in their overall health, prosthetic satisfaction and physical function in the last 4 weeks. Next, using the 3 separate global change scales, subjects will rate the amount of change they have experienced on a scale of -7 (much worse) to +7 (much better). Use of global change ratings has face validity, as retrospective appraisal by the patient is widely used in clinical practice to assess change and has been found to be highly correlated with treatment satisfaction.<sup>26</sup>

This work is designed to provide parameters for the continued evaluation of prosthetic and rehabilitation interventions that will help physicians, clinicians and patients establish shared values for outcomes measurements that are statistically valid and that can be tracked over time. Ultimately, the goal is methodologically sound clinical trials and assessment instruments that will improve patient care even as they allow researchers, prosthetists and physical therapists to monitor, track and assess information about limb function, overall mobility, and prosthetic satisfaction.

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# Blast Injuries In Civilian Practice

Christopher T. Born, MD, FAAOS, FACS, Ryan Calfee, MD, Joann Mead, MA

**ALTHOUGH EXPLOSIONS UNRELATED TO TERRORISM** occasionally occur in industrial settings, within today's geopolitical environment explosions and bombings are all too commonly the primary disaster "events" to which both civilian and military medical/surgical personnel routinely must respond. Indeed, data from the RAND@-MIPT Terrorism Incident database show that bomb blast injuries worldwide account for 82% of all injuries caused by terrorists. (Figure 1)

As terrorists expand their operations, injuries from blast are unfortunately becoming more common in the non-military population. Recent terrorist incidents such as Oklahoma City in 1995,<sup>2</sup> Atlanta's Centennial Olympic Park in 1996,<sup>3</sup> Manchester, England in 1996,<sup>4</sup> the multiple bombings in Madrid, Spain in 2004,<sup>6</sup> and the train and bus explosions in London on July 7, 2005,<sup>6</sup> have provided investigators much opportunity to study blast injury in greater detail. Out of necessity, the military has expanded its understanding and ability to manage blast-related injuries. However, the civilian medical community remains relatively unprepared. In a membership survey conducted by the **Eastern Association for the Surgery of Trauma (EAST)**, only 73% of the trauma surgeon-respondents felt that they had an adequate understanding of the pathophysiology and classification of blast injuries.<sup>7</sup>

This knowledge is crucial. Knowledge of the blast scene and blast mechanics can improve triage at the disaster scene and/or in the emergency room. In addition, triage teams trained to respond to blast scenarios can determine how efficiently potentially scarce or overburdened local resources are utilized. One remarkable example was the response to the simultaneous detonation of 10 explosions on commuter trains in Madrid, Spain on March 11, 2004: 177 people were killed at the scene; over 2000 were wounded.<sup>9</sup> Of this number, 966 civilians were transported to hospitals. Gregorio Maranon University General Hospital, which was closest to the disaster scene, received 312 patients, 91 of

whom were hospitalized. Resources employed for this event reportedly included more than 70,000 health personnel, 291 ambulances, 200 firemen, 13 psychology units, 500 volunteers, and thousands of blood donors. Emergency communication centers received over 20,000 calls that morning. At Gregorio Maranon alone, 272 victims were treated between 8:00am and 10:30am. In immediate response to the blast, all surgeries in 22 operative suites were cancelled and 161 patients were discharged in 2 hours.<sup>9</sup>

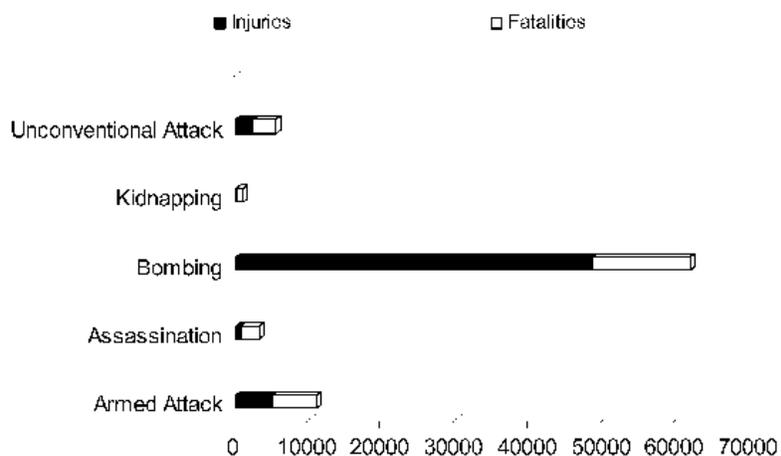
Triage errors are categorized as *undertriage* or *overtriage*. Undertriage is the assignment of critically injured casualties needing immediate care to a delayed category. This may lead to preventable deaths. It can be avoided by training triage officers to recognize life-threatening problems requiring urgent treatment. Overtriage is the assignment to immediate care, hospitalization or evacuation of those casualties who are not critically injured. This potentially displaces more critically injured victims from medical resources. The overtriage to Gregorio Maranon hospital was estimated to be >50% with 0% undertriage. This trend of overtriage to nearby hospitals replicates reported experiences in other incidents.<sup>3,10,11</sup> Fortunately, the Madrid

trauma center rapidly adapted to the situation. When medical resources are limited, or not immediately available, overtriage can prove as deadly as undertriage for victims awaiting treatment.<sup>10</sup> Even in Madrid, the triage might have proven disastrous if the attacks had not occurred in the early morning, when the full day staff of the hospital was arriving and the operating rooms were prepared for the day's first cases, but not yet occupied.

There are numerous triage algorithms used in the management of blast victims. Although the scoring systems vary, each is designed to provide responders with an easily remembered way to evaluate patients with high inter-rater reliability. These systems provide a structured framework for rescuers working in a chaotic environment. However, there is no single approach, especially if "dirty bombs" complicate triage efforts following blast events.<sup>8</sup> In these latter situations, an assessment of the safety and the exposure risk of rescue personnel along with the risk of contamination of health care workers and facilities must be considered before rescue efforts commence.

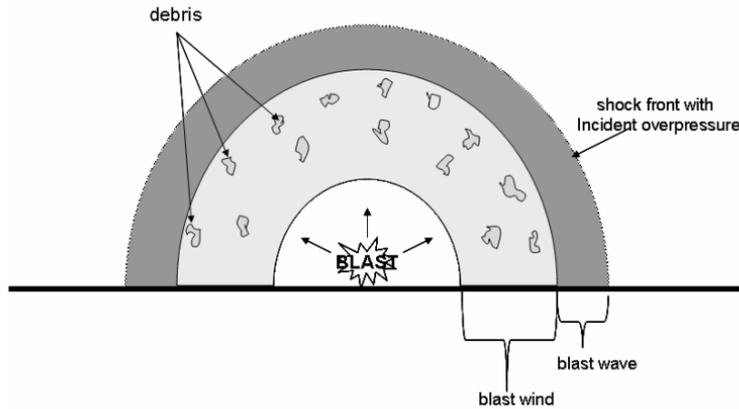
Contrary to the common sense assumption, the great majority of survivors of bombings are not critically injured. In

**Figure 1: Terrorist Injuries and Fatalities 1998-2005**



Data from the RAND@-MIPT Terrorism Incident database show that bomb blast injuries account for 82% of all injuries caused by terrorists.<sup>1</sup>

**Figure 2: Diagram of blast wave and associated components**

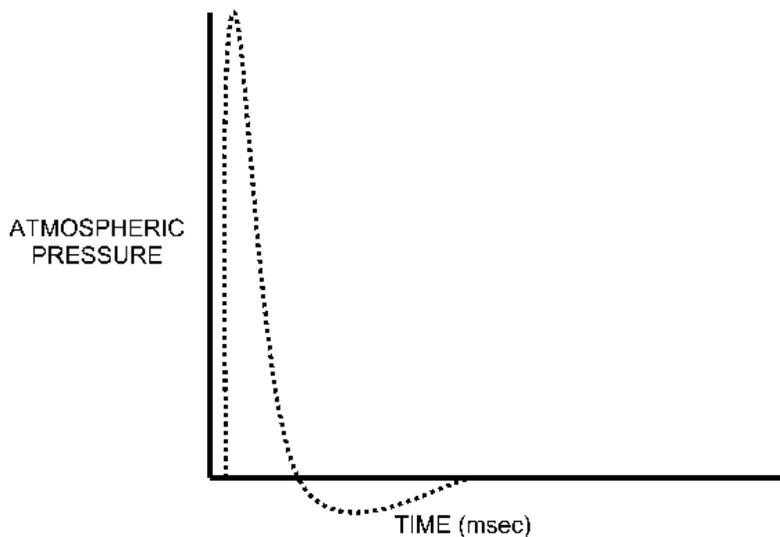


Air is highly compressed on the leading edge of the blast wave creating a shock front. The body of the wave, including the associated mass outward movement of air (sometimes called the "blast wind") follows this front. (After Hull JB. Blast: injury patterns and their recording. J Audiovisual Media in Med. 1992;15:121-127)

part, this is due to the sobering fact that the immediate death rate from blast exposure tends to be high, ranging from 50% - 99%. Those who do survive commonly suffer soft tissue and musculoskeletal injuries, most of which are non-critical and non-life threatening. Critical injuries occur in only 5% - 25% of survivors, and late deaths generally occur in this severely injured group. Nineteen percent of all survivors with abdominal

trauma, 14% of all survivors with chest trauma, and 10% of all survivors with traumatic amputation or blast lung injury ultimately die, representing the body system injuries with the highest specific mortality among survivors. However, these body system injuries are found in only a small (2% - 5%) percentage of survivors because most victims with these injuries died immediately before reaching medical care.<sup>12</sup> In appropriate tri-

**Figure 3: Blast wave form**



In an open area, the overpressure that results from an explosion generally follows a well-defined pressure/time curve ("Friedlander wave") with an initial near instantaneous spike in the ambient air pressure followed by a longer period of sub-atmospheric pressure.

age, survivors with these injuries are recognized early as having a high risk of death.

These percentages have a direct impact on ongoing efforts to improve the accuracy of field triage and optimize health care resource utilization following blasts. Recent research into triage markers based on a survey of soldiers in Iraq found that sustained hypotension and the presence of two or more factors, including three or more long bone fractures, penetrating head injury, and associated fatalities are associated with increased mortality.<sup>13</sup> A review of suicide bombings in Israel sought to define easily identified external injuries that correlated with the development of blast lung injury.<sup>14</sup> In 798 victims, significant associations ( $p < .001$ ) with the development of blast lung were found between penetrating wounds to the head or torso, burns greater than 10% of the body surface area, and skull fractures. Additionally, victims in fully confined spaces, such as buses, were more likely to suffer blast lung effects. These findings provide rapid ways to identify patients who will likely require more intensive monitoring and resuscitative efforts even before the clinical manifestations of pulmonary compromise become apparent.

Specifically, triage methodologies must take into account three primary components as they interface either directly or indirectly with the victim. These include the high-pressure shock front and associated blast wave as well as any thermal components from the detonation. Classically, the injuries have been divided into three categories (primary, secondary and tertiary). We have also come to also recognize several quaternary elements.

**Primary blast injury (PBI)** occurs as the shock front and blast wave move through the body. Differences in densities of the body's anatomical components (particularly at air/fluid interfaces) are susceptible to spalling, implosion, inertial mismatches as well as pressure differentials. Spalling describes the forcible, explosive movement of fluid from more dense to less dense tissues. This is common in the lungs. Implosion relates to areas of gas that rapidly compress at the time of shock front impact and then rapidly re-expand after the front passes. This

is frequently seen in the ear (tympanic membrane) and intestine, where acceleration/deceleration can cause tearing of organ pedicles and mesentery when there is an inertial difference between organ structures. Pressure differentials can occur wherever there is a liquid/gas interface. Incompressible or fluid filled organs (e.g. vessels) may then be injured when their fluid content is forced into a less compressible, adjacent structure.

Bomb detonation is the rapid chemical transformation of a solid or liquid into a gas. The gas expands radially outward in the form of a high-pressure shock wave that exceeds the speed of sound. Air is highly compressed on the leading edge of the blast wave creating a shock front. The body of the wave, including the associated mass outward movement of air (sometimes called the "blast wind") follows this front.<sup>15</sup> (Figure 2) In an open area, the overpressure that results generally follows a well-defined pressure/time curve ("Friedlander wave") with an initial near instantaneous spike in the ambient air pressure followed by a longer period of sub-atmospheric pressure. (Figure 3)

Since the pressure/time curves vary depending on the local topography, (e.g., the presence of walls/solid objects and whether the blast is detonated indoors or outside), knowledge of the physical parameters of the explosive arena is critical to triage analysis. In contained explosions, the blast wave can reflect off of and flow around solid surfaces resulting in magnification of pressure up to 8 or 9 times, causing significantly greater injury.<sup>15,16</sup>

Although high-energy explosives such as TNT and **nitroglycerin (NTG)** are much more powerful than ordinary gunpowder, gunpowder's high thermal output typically causes more burn injuries. In comparison, TNT and NTG are cleaner and more complete in combustion. They are, however, more devastating because they create shockwaves of higher energy, causing other injuries besides burns.

This information is obviously important for medical teams evaluating blast injuries. Likewise, medical teams should understand how the medium through which the blast wave moves also impacts the type and severity of injuries. Here, it should be noted that any explosion has

the potential to be associated with nuclear, biologic or chemical contaminants, and this should also remain a consideration for healthcare givers until proven otherwise.<sup>17</sup>

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## **Critical injuries occur in only 5% - 25% of survivors, but late deaths generally occur in this severely injured group.**

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Water, with its increased density, allows for faster propagation and a longer duration of positive pressure accounting for increased severity in that environment. The distance from the explosion's epicenter is important, with pressure wave decay occurring roughly as the inverse cube of the distance traveled.<sup>15,18</sup>

Since the most susceptible organs to primary blast injury are the ears, lungs and gastrointestinal tract, tympanic membrane rupture should also be used as a triage marker for exposure to significant blast overpressure. The lungs are moderately more resistant, but with enough energy exposure the air sacs can be disrupted and local capillaries can hemorrhage, leading to emphysematous spaces and pneumothorax. The interstitial changes of blast lung can lead to **Adult Respiratory Distress Syndrome (ARDS)**. Notably, infiltrates can be seen on chest X-rays within 90 minutes of the blast.<sup>19</sup> In rare cases, air embolism of the vascular tree is thought to lead to sudden death.<sup>20</sup> The gastrointestinal tract as a gas filled organ can be injured by implosion and rupture. The mucosal wall can become bruised. Shearing injuries can also occur, caused by acceleration/deceleration relative to more solid, adjacent structures. Other organ systems have varying degrees of response to injury from primary blast and models have been developed to better study the overall pathophysiological effects.<sup>15,20,21,22</sup> The lungs tend to be the predominant nonauditory system injured in most air blasts, whereas the **gastrointestinal (GI)** tract is more susceptible to underwater blasts. Histochemical markers are being sought to better diagnose and treat blast overpressure injury.

Amputations are not common, but can infrequently result from laceration by projectiles formed secondary to the blast, which are significant as markers for potentially lethal injuries. These primarily occur through the shaft rather than as disarticulations and are thought to be the result of direct coupling of the blast wave into the tissues. Although somewhat controversial, it is theorized that fracture results from axial stress to the long bone and flailing of the extremity from the blast wind gas flow completes the amputation.<sup>18,23</sup> Improved knowledge in this area has allowed for the development of more effective body armor.

Secondary blast injury results from the victim being struck by missiles that are propagated by the explosion (shrapnel). These might include the bomb's casing or materials that have been intentionally imbedded into the explosive to cause wounding (*primary fragmentation*). Nails, screws, nuts and bolts seem to be a favorite of terrorists. *Secondary fragmentation* describes local material made airborne by proximity to the explosion (e.g. glass). Most penetrating injuries caused by blast-driven projectiles should be considered as contaminated and prophylaxed with antibiotics and tetanus. Small entry holes may be misleading and decisions regarding which wounds to explore and debride may be difficult. X-ray evaluation should be liberally used to look for foreign bodies. There have been reported instances of wounding by allogenic bone fragments from suicide terrorists or other victims that have become imbedded in survivors. These cases require special management with attention to potential disease transmission.<sup>24</sup>

Tertiary injury stems from the victim's body being thrown as a projectile by the blast. This can result in fractures, head trauma and other blunt injury typically seen in the surviving population. Quaternary injury encompasses damage from structural collapse or burns secondary to the detonation. Crush, traumatic amputation, compartment syndromes in addition to other blunt and penetrating injuries can be common sequelae of structural collapse. Flash burns to exposed skin can occur as a result of the thermal component of the detonation. Secondary fires can cause additional burns as well as smoke inhalation.

In conclusion, civilian physicians and surgeons need increased understanding of blast injury, since early, accurate assessment—based on knowledge of blast mechanics and patterns of blast injuries—has the potential to improve triage efforts and increase survivorship. Although injury from flying debris can be lethal, the vast majority of blast survivors are not critically injured; thus, the challenge facing the medical community is to effectively identify and treat those few casualties with severe injuries. To that end, information regarding the explosion type, physical environment, and typical factors contributing to blast injuries all have a direct impact on triage evaluation. Given that most civilian medical professionals have not been involved in true mass casualty blast events, continued education and advance planning will provide the cornerstone to coping with future blast events.

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# CME Background Information

This CME activity is sponsored by Brown Medical School.

**Target Audience:** This enduring material is designed for physicians licensed in Rhode Island.

**Educational Objectives:**

1. Readers will know the new materials and new properties of biohybrid limbs.
2. Readers will know the new advances in regenerative medicine [engineering tissue and organ replacements] for limb trauma.
3. Readers will describe the latest biomimetic prostheses.
4. Readers will know the latest information on development of neuromotor prostheses.
5. Readers will identify clinically meaningful improvement in the rehabilitation of lower-limb amputees.
6. Readers will know the facts about prevalence of blast injuries among civilians, and triage protocols.

**Needs Assessment:** The incidence of massive civilian casualties, and injuries, from terrorist-activities and US engagement in warfare dates from the past 5 years. Physicians today are seeing more bombing-related limb injuries. This issue aims to update physicians on the kinds of injuries that are occurring, and the new treatment options that have been developed, and are in the process of being developed.

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Keep a copy for your files. Compare them with the correct answers, which will be made available upon request, and receipt of submission requirements.

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| * I know the latest information on development of neuromotor prostheses.  | 1 2 3 4 5  |
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## THE BIOHYBRID LIMB: CME QUESTIONS

Please circle the single correct answer for each of the questions below:

- Which of the following statements about the concept of the biohybrid limb is *not* true:
  - Current examples of biohybrid limbs include bone and joint replacements, engineered skin, osseointegrated transcutaneous implants, cardiovascular grafts, and neuro-prosthetics.
  - Biophysical properties result from the interface between non-biological and biological tissues.
  - Titanium joint replacements have raised serious concern with researchers because of the complications that result from the integration of titanium with bone.
  - Conceptualizing a limb as a biohybrid organ can free the researcher from constraints imposed by certain limitations of biomaterials.
- If researchers succeed in developing an environmental seal by integrating skin and dermis with titanium, they could potentially accomplish which *one* of the following:
  - A decrease in percutaneous contamination
  - A decrease in titanium oxide surface film
  - An increase in growth factor secretion
  - An increase in marsupialization
- Which of the following provides the theoretical basis for using growth factors to stimulate endogenous repair and to facilitate cell-mediated engineered repair:
  - Unique biophysical properties result from the interface between non-biological and biological tissues.
  - Many of the same signaling molecules that regulate cartilage development in embryogenesis are re-expressed in post-natal life during tissue growth and repair.
  - Synovium has a demonstrated propensity to undergo chondrogenesis and contains a mixed population of cells that respond differently to various growth factors.
  - TFG- $\beta_1$ , when combined with IGF-1, can dramatically improve chondrogenesis compared to the supplementation of TFG- $\beta_1$  alone.
- Since delayed bone union complicates rehabilitation and restoration of limb function after distraction osteogenesis, tissue engineering research is exploring all of the following avenues *except*:
  - Progressive weight-bearing
  - Using growth factors and biopeptides to stimulate healing
  - Low intensity ultra sound radiation
  - Neuro-motor bone implants
- The most radical improvement in prosthetic knee joint technology in the 1970s was
  - A decrease in percutaneous contamination
  - Mechanical power generation
  - The Series Elastic Actuator
  - Active variable damping
- Which of the following is *not* a problem for lower limb amputees who are using commercially available prosthetics (i.e., prosthetics that are not yet capable of fully restoring natural limb function).
  - Increased osseoperception
  - Difficulties maintaining balance when walking, especially over rough terrain
  - Impaired metabolic economy and resultant undue fatigue
  - Lack of direct response to amputee intention (i.e., when an obstacle appears in a pathway or the intention to turn right or left)
- Neuromotor prosthesis (NMP) technology has the potential to
  - accumulate, synthesize and store data about the user's usage, including metabolic rates, gait patterns and variable damping rates
  - enable direct two-way interaction between the human brain and a mechanical prosthesis
  - stimulate cortical "spikes" that will release naturally present growth factors to catalyze chondrogenesis.
  - decode cortical "spikes" that will stimulate endogenous repair and/or facilitate cell-mediated engineered repair
- Which of the following statements about the miniaturized brain implantable NMP technology now under development is *not* true:
  - It is compatible with the longer term goal of connecting motor cortex signals to external prosthetic devices.
  - It is compatible with the longer term goal of connecting motor cortex signals to muscle nerves via a fiber optical network within the body.
  - It is capable of providing direct brain control of artificial limbs for amputees.
  - It is flexible and scalable to allow transmission of large amounts of neural information from the cortex to assistive technologies (such as a prosthesis, a wheel chair, or a computer cursor).
- For assessment measures, minimum detectable change (MDC) is defined as
  - the minimum amount of change that exceeds measurement error
  - the threshold at which an individual has experienced a clinically relevant change.
  - the ability of an instrument to detect clinical change as judged by an external criterion.
  - a single value applicable across all patients.
- Which of the following does *not* create problems for the assessment of amputee prosthetic satisfaction, quality of life and mobility:
  - Some assessment tests lack the psychometric properties that enable them to detect change on the individual level.
  - Individual self-report assessment measures do not currently exist for amputees.
  - Some assessment tests in this realm have shown strong floor and ceiling effects.
  - Many current assessment measures that work well with large groups do not work on individuals or small groups.
- In assessing blast victims (during triage and emergency room screening) medical personnel should know that victims of abdominal trauma, chest trauma and lung injury
  - are likely to be fewer when the blast takes place underwater
  - are likely to be fewer when the blast takes place in a confined space
  - have the highest rates of mortality
  - have the lowest rates of mortality
- According to the essay on blast injuries, in comparison with ordinary gunpowder, TNT and nitroglycerin (NTG)
  - are less clean and less complete in combustion
  - have a lower thermal output (which means that victims of gunpowder blasts will typically have fewer burn injuries).
  - are more devastating because they create shockwaves of higher energy, causing other injuries besides burns.
  - are more common in blast explosions

# Using the Comprehensive Clinical Approach to Older Patients

Ana C. Tuya, MD, and Richard W. Besdine, MD

An 84-year-old woman comes to your office for routine follow up. Her problem list includes osteoarthritis and hypertension. She has no specific complaints on presentation, but you note she is using a cane for the first time since you've known her. On specific questioning, she reports several weeks of worsening of her chronic lower extremity edema, and increased difficulty climbing stairs and walking long distances. In fact, her daughter has begun doing her food shopping. She says she's doing better with the cane, and her left knee pain is better since she started using over the counter Advil about one month ago.

This patient illustrates common dilemmas presented by complicated older adults with functional decline of unknown etiology in the face of multiple co-morbidities. Caring for the older adult requires the skills of a good physician and of a talented detective; disease in old age can present without classic or typical findings. The aging of the baby boomer generation, along with increases in life expectancy and medical advances, are producing stunning increases in the population of older Americans—over 65, over 75 and especially those over 85. Projections from the US Census Bureau estimate approximately 90 million Americans over the age of 65 and almost 20 million persons over 85 by the year 2050. Knowing some of the key principles of care and treatment for older adults will be useful for all physicians and practitioners, regardless of specialty or patient population, excluding only pediatricians. The aging imperative brings with it the challenge and excitement of caring for a complex patient population, in whom atypical presentations abound, and where small interventions often bring large and rewarding results for both patient and physician.

The goal of this column is to provide clinicians with 1) case-based learning and reinforcement of basic principles of Geriatrics, 2) updates on new treatment options for conditions of interest, 3) tools for use in daily practice, and 4) resources for further learning and for teaching students. Community referral sources, web-based teach-

ing tools and learning resources will be provided. Topics will include outpatient care and prevention, nursing home medicine, and inpatient acute care.

Among healthy older adults, homeostasis is maintained in fine balance, just as in younger persons. The crucial difference is that changes in organ reserve, due to aging alone, are common, and lead to restricted capacity to maintain that homeostasis when stressed. Sometimes called “homeostenosis” (a made up but vivid word), the concept is critical to understanding older persons. Only modest severity of physical illness, drug toxicity or trauma often results in catastrophic declines, leading to a cascade of seemingly unrelated problems (pneumonia presenting with confusion, falling, urinary incontinence and loss of self-care capacity). In such circumstances, recognition of the underlying trigger is challenging, especially if evaluation is limited to the organ with obvious symptoms – brain in confusional states, urinary tract for incontinence, and motor system for falls. Finally, multiple comorbid conditions, changes in pharmacokinetics and pharmacodynamics, and the changes of pure aging lead to additional levels of complexity.

Hence, the tool of **comprehensive geriatric assessment (CGA)** has been developed to provide systematic assessment of the older adult to detect subtle changes, and to avoid missing important areas for intervention. The goal of CGA is to create a multidisciplinary care plan that will anticipate problems and prevent illnesses and functional decline; the ultimate goal is preservation of independence. Since CGA can consume a full new patient visit, quick screening (5 minutes) can be used to identify any needs for further assessment. CGA and screening can be especially useful when evaluating a new patient or when a new stressor, diagnosis, or transition in level of care has occurred. The basic components of CGA include assessment of physical function (ADL, IADL, Timed Up and Go test, and balance testing), affect (geriatric depression scale), cognition (MMSE, Mini-

cog) and assessment of social supports and living situation.

The **activities of daily living (ADL)** include toileting, feeding, dressing, grooming, walking, and bathing. The **instrumental activities of daily living (IADL)** include telephone use, shopping, food preparation, housekeeping, laundry, transportation, and medication and finance management. In adults 65-74 years old, 15% describe one or two ADL dependencies, and 11% describe needing assistance with IADL. For those 85 and older, the percentages increase to 13% requiring assistance with IADL and 27% with ADL decline<sup>1</sup>. Performing an Up and Go test (rise from a chair, walk 10 feet, turn, walk back and sit) can provide useful information about fall risk and balance. If the patient takes longer than 9 seconds to perform the test, falls risk is increased; such patients would benefit from physical therapy assessment for interventions. If time does not permit formal measurement of the test, then simply watching the patient walk, such as when going from a chair to the exam table is also useful.

Depression screening is recommended; although not more common with age, under-reporting and much lower detection rates are reported. One-quarter of older adults acknowledge depressive symptoms, but only 1-9% meet DSM criteria for major depression<sup>2</sup>. The geriatric depression scale has a short form of 15 questions that can be administered quickly. Impaired psychosocial function predicts morbidity, mortality and functional decline. Cognitive assessment should also be performed at least yearly and during any new visit. The Folstein MMSE can be used, but many practitioners are using the Mini-Cog (three-item recall and clock drawing) as a quicker screen. Asking about other losses of function is also useful; e.g., incontinence, hearing, nutrition. Older patients may assume that symptoms in these domains are part of “normal aging,” and often do not complain. The above tools collect important information about an older adult's risks for functional decline and any need for alteration in living situation; their use also detects func-

tional decline early, allowing intervention before harm occurs.

Now let's return to our patient; she presents with new functional decline, triggering CGA. Is this decline due to worsening lower extremity edema, or is it due to the recent flare in her left knee osteoarthritis? Did Advil contribute? Additional history indicates that she remained independent until a month earlier, when her knee pain flared. Prior to this flare, she used the bus to go shopping, did her own housework and was able to climb steps without limitation. After the knee pain worsened, she began using Advil daily. Her daughter took over grocery shopping, and the patient began using her deceased husband's old cane for support.

CGA spotlights the functional decline, which seems related to her increased venous stasis edema. While observing the patient move toward the exam table, you notice that her cane is too long for her—the handle at least 6 inches higher than the ulnar styloid of her arm when it is fully extended perpendicular to the ground. In addition, she uses the cane with the left hand—canes should be held in the arm on the side opposite the painful or weak lower extremity. You and the patient agree to stop the Advil, since it seems to be contributing to her fluid retention and increased edema, and try Tylenol around the clock. She agrees to physical therapy, where a new cane is fitted, she is instructed in its use and strengthening exercises are begun. Two weeks later, she reports that she no longer needs the cane and is able to use the bus to do her own shopping again. The edema has significantly improved as well, and she is thrilled to have regained her ability to live independently.

A parallel ending to this case could be described; imagine the same patient presenting to her physician's office with improved osteoarthritic pain on Advil, and ambulation with the cane. A physician not familiar with CGA might have overlooked the improper fit of the cane and the significance of the functional decline, and no evaluation would have occurred. With continued Advil use, a different scenario is plausible. The patient remained stable for several months, but had progression of her edema and further restricted her activities. She started to rely on her daughter for help with housework and cooking. One evening she developed shortness of breath and orthopnea and called rescue. She was admitted for fluid retention and CHF, and treated with Lasix and oxygen, with improvement. However, while in the hospital she developed delirium secondary to electrolyte imbalance and dehydration from excess diuretics, fell and fractured her left hip. Surgery was successful, and she was discharged to a nursing home for rehabilitation after her delirium cleared. Because she never regained pre-fracture mobility, and because she could no longer manage her medications independently due to lingering cognitive deficits, she became a permanent resident of the nursing home.

The failure to recognize the significance of a seemingly small decline in function, and to anticipate its possible consequences, led to the uninterrupted cascade of decline, resulting in loss of independence and further co-morbidities with increased mortality risk. Delirium and hip fracture both carry substantial increases in mortality. The mortality rate for delirious hospitalized patients ranges from 22-76%, and the increased risk persists for up to a year<sup>3</sup>. One-year mortality for hip fracture is 15-25% in women, and higher in men. Most significantly, this version of our patient's story ends with her permanent placement in a nursing home—an outcome greatly feared by most of us.

The goals of geriatric care are to promote successful aging,

to prevent and reduce disability, and to preserve independence. CGA provides a toolkit that can highlight disability early and generate a comprehensive multidisciplinary care plan that will anticipate and prevent clinical catastrophes and interrupt the cascade of decline. The principles learned from assessment research can be implemented in the busy office practice and can be streamlined to fit the physician's needs. Take home questionnaires, pre-visit forms, and home assessments by occupational therapy or nursing can gather many of the elements for assessment and care planning when indicated by the office evaluation. Finally, community resources can be of tremendous assistance to a busy practitioner with limited support. The following are sources of referral and on-line resources for the tools allowing you to perform CGA on a routine basis.

## RESOURCES

1. Resources for Geriatric Education: Web based toolkit with relevant screening tests, instructions on assessment and scoring, and the necessary forms in PDF links, articles and useful websites for practitioner support.  
<http://www.chcr.brown.edu/toolkit.htm>
2. AGS-sponsored pocket text for Geriatrics, now available as PDA-based and on-line.  
<http://www.geriatricsatyourfingertips.org>
3. Division of Geriatrics Faculty 444-5248
4. East Avenue Geriatrics Practice for referrals 728-7270
5. Reynolds Project Resource Center for Geriatrics Education (RCGE) 863-3211
6. American Geriatrics Society  
<http://www.americangeriatrics.org>

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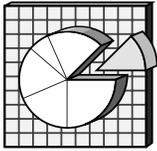
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## Birth Defects In Rhode Island

*Samara Viner-Brown, MS, and Meredith Bergey, MSc, MPH*

**Birth defects are structural abnormalities** that affect the development of organs and tissues of an infant or child. These abnormalities may be identified during pregnancy, at birth or following birth. Possible causes or contributing factors to birth defects include genetic factors, environmental pollutants, occupational hazards, dietary factors, infections, medications, and personal behaviors.<sup>1</sup> In both the United States and Rhode Island, birth defects are a leading cause of infant mortality and contribute to childhood illness and disability. However, early recognition and response to birth defects may often prevent more serious effects.

Rhode Island began developing a birth defects surveillance system in 2000, with funding from the **Centers for Disease Control and Prevention (CDC)**. During 2003, the Rhode Island General Assembly enacted legislation (Rhode Island General Law 23-13.3) requiring the development and implementation of a birth defects reporting, surveillance and information system by the Rhode Island Department of Health. The Rhode Island Birth Defects Program, created in response to this mandate, is designed to track the prevalence of birth defects among children ages 0 – 5 in Rhode Island and collect information on the characteristics of those children and their parents, assure that those children and their families receive appropriate services and referrals, and identify and close gaps in services for families of children with birth defects. This report presents selected summary data from the Birth Defects Program for the years 2001-2005.

### METHODS

Data on birth defects in the Rhode Island population are collected in two ongoing data sources maintained by the Department of Health: birth certificate data collected by the Office of Vital Records and hospital discharge data collected by the Center for Health Data and Analysis. Birth certificate data include a wide variety of information on the characteristics of the child, parent, and birth experience, but may not capture all birth defects and does not identify birth defects at the level of detail in the **International Classification of Diseases coding system (ICD-9-CM)**.<sup>2</sup> Hospital discharge data include a record for nearly every birth occurring in the state and code all recorded birth defects in ICD-9-CM, but collect few data items on the characteristics of the child and parents. Therefore, the Birth Defects Program uses hospital discharge data to identify newborns with birth defects and links their hospital records with their birth certificate records. In addition to case identification through the hospital discharge database, the Birth Defects Program is working with Women & Infants Hospital, Rhode Island Hospital, and Hasbro Children's Hospital to obtain additional cases of birth defects and information on services provided to families of children with birth defects. To determine whether children with birth defects receive appropriate preventive services, the Birth Defects Program links children identified with birth defects to

Rhode Island's integrated child health information system, KIDSNET. Since KIDSNET maintains information from ten program databases, children who are not receiving services can be identified and provided outreach and referrals.

### RESULTS

Among the 61,870 Rhode Island babies born in the state's maternity hospitals during 2001-2005, hospital discharge data indicate that 3,510 (5.7%) had at least one birth defect. By year, the number of newborns with birth defects ranged from a low of 691 in 2001 to a high of 720 in 2005. Overall, the statewide prevalence rate per 10,000 births for birth defects has remained stable over the past five years, varying within a range of only 7% around the five-year average rate of 567 babies per 10,000. (Figure 1)

Birth defects have been reported in all organ systems among Rhode Island newborns during 2001-2005. (Table 1) The most frequent birth defects are those related to the cardiovascular system, where one in 40 babies are born with a cardiovascular de-

**Table 1.**  
Prevalence of Birth Defects by Body System  
Rhode Island, 2001-2005

Organ System	Number	Prevalence Rate per 10,000 Live Births*
Cardiovascular	1487	240.3
Musculoskeletal/Integumentary	1368	213.3
Genitourinary	834	134.8
Gastrointestinal	306	49.5
Eye, Ear, Face and Neck	217	35.1
Central Nervous System	149	24.1
Chromosomal	107	17.3
Respiratory	88	14.2

\*Because newborns may have birth defects in more than one organ system, the prevalence rates for organ systems add to a total that is greater than the overall prevalence rate of 567 per 10,000 live births.

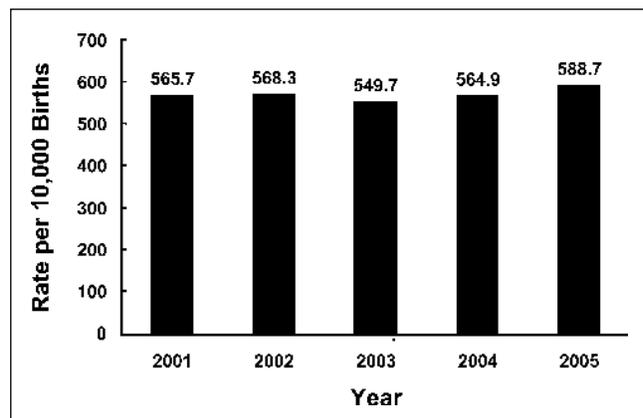


Figure 1. Newborns with birth defects per 10,000 live births, Rhode Island, 2001-2005.

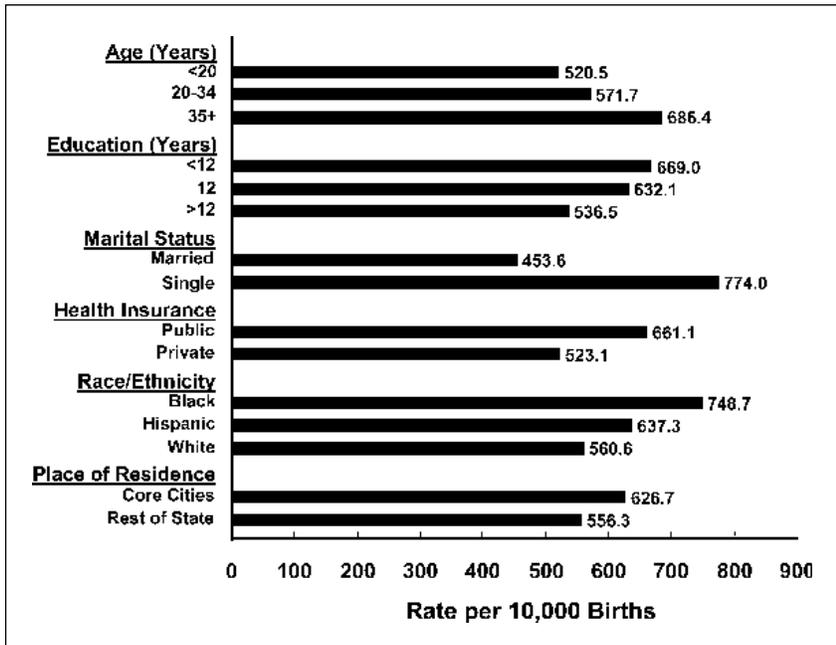


Figure 2. Newborns with birth defects per 10,000 live births, by selected maternal characteristics, Rhode Island, 2005.

fect. Also common are birth defects affecting the musculoskeletal and integumentary systems and the genitourinary system.

The prevalence rate for birth defects varies with maternal characteristics. Babies born to older women (ages 35 or greater), women with less than a high school education, single women, women with publicly funded health insurance, or women of color, are at a higher risk for birth defects. (Figure 2) During 2005, the birth defects rate among women aged 35 or greater was 686.4 compared to 520.5 among women aged less than 20. Similarly, the birth defects rate among women with less than a high school education (669.0) was 1.25 times the rate among women with more than a high school education (536.5). Single women (774.0) were nearly twice as likely to have a baby with a birth defect than married women (453.6). Women who were insured through public programs such as RIte Care and Medicaid were also more likely to have a baby with a birth defect (661.1) than women insured by commercial or private providers, such as Blue Cross and United Healthcare (523.1). Black/African American women were more

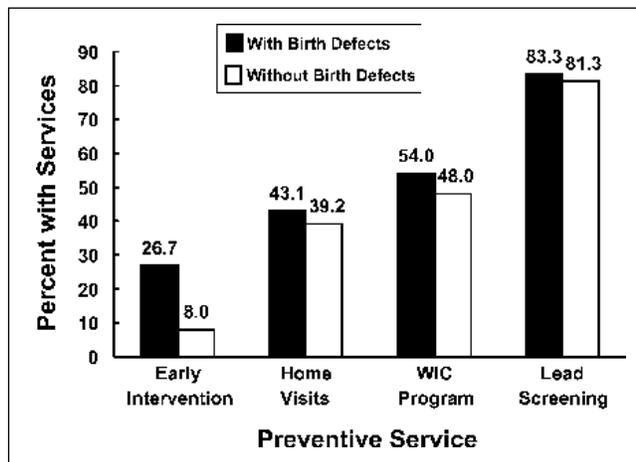


Figure 3. Newborns receiving selected preventive services, by diagnosis of birth defects, Rhode Island, 2004.

likely to have a baby with a birth defect (748.7) than White women (560.6). Birth defect rates were also higher among those who resided in the core cities, including Central Falls, Newport, Pawtucket, Providence, West Warwick and Woonsocket (626.7 per 10,000 newborns) than those who lived in the rest of the state (556.3).

Data indicate that among Rhode Island children born in state during 2004, a higher proportion of children with birth defects were screened for lead poisoning, were enrolled in the state's WIC and Early Intervention programs, and received home visits compared to children without birth defects. (Figure 4)

## DISCUSSION

Over the last five years, 5.7% of newborns in Rhode Island, or approximately 700 per year, have been diagnosed with birth defects. Nationally, the reported prevalence rate is much lower, at 3.0%.<sup>3</sup> However, because there are no national uniform standards for case ascertainment, it is difficult to compare rates across states. For example, some state registries use active surveillance (i.e., a case finding process where cases are identified at multiple data sources and includes identifying potential birth defect cases, medical record abstraction and follow-up), while others use passive surveillance (i.e., wait for data to be submitted to the program by limited data reporting sources), and still others use a combination of passive and active systems.<sup>4</sup> Also, some states limit their registries to live birth outcomes while others may also include fetal deaths. Although Rhode Island is working to make its case ascertainment system an active one, the system currently is passive and does not include data on fetal deaths.

Once birth defects cases are identified, the Rhode Island Birth Defects Program works to assure that these children and their families receive appropriate services and referrals. The Program also has been conducting focus groups, interviews and surveys with families to learn about their experiences with the health care system and to determine any gaps in or barriers to the system. This information will be used to develop strategies that will help link families to follow-up and treatment services, which hopefully, will lead to a reduction in disparities.

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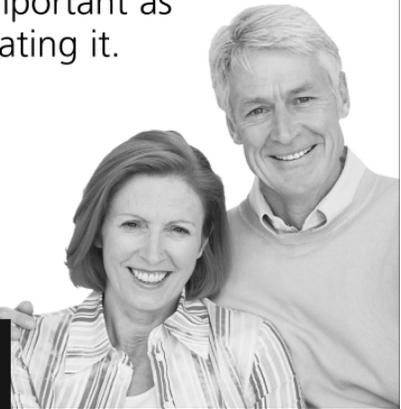
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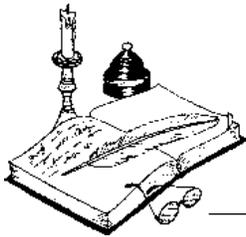
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# Physician's Lexicon

## A Nervous Assortment of Words

The histologic structure of the central nervous system was the last of the major organs to be clarified. Anatomists had clearly portrayed the cellular architecture of most of the internal organs of the body by the middle decades of the 19th Century. The brain, however, was refractory to the early histologic stains and was therefore thought of as an ill-defined syncytial soup, lacking in discreet cellular membranes. This view prevailed until the meticulous microscopic studies of Golgi, and particularly Cajal, both of whom used metallic impregnation stains to demonstrate the cellular components within this mysterious "soup." Cajal then defined the anatomy of the neuron, its numerous cytoplasmic extensions, its synaptic intimacies and from its linear configuration he then inferred the unidirectional character of its signaling capabilities.

The root, neuro- [as in neuron] comes

from a Greek word meaning sinew or tendon; and from a still earlier term meaning vigor. The derivative Latin, *nervus*, became the direct source of the many English words pertaining to neural activity [neuroglia, neurology, neurosis, neurotransmitter, neurasthenia, etc.]

The word, nucleus, is derived from the Latin, *nuculeus*, meaning little kernel, which in turn is from the Latin, *nucis*, meaning nut.

Axon, the major efferent limb of the neuron, is from a Greek word meaning axle. Cognate words in English include axis, axil [the angle between a leaf and its branch] and axillary [a Latin term meaning armpit, referring to the angle formed by the arm and lateral thorax.] And, via the Anglo-Saxon tongue, the words, aisle, aileron and alar.

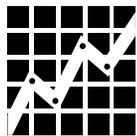
Dendrite is also a derivative of a Greek word, the *dendro-* root meaning tree, branch or root. The term appears in such words as

rhododendron [red roots], dendrology [the study of trees], dendrolite [fossil plants; literally, a stone tree], oligodendroglia [glial cells with a paucity of branches] and epidendrum [a genus of tree orchids.]

Synapse is derived from the Greek word, *synaptein*, meaning to bind together. The *syn-* prefix means with or together and appears in words such as synarthrosis [fused joint], synchronize, syncytium [a joining of cells], syndrome, [a running together], synod, syndicate, synonymous, synergy and syncope [in medicine, a fainting spell; in music, a displacement of a beat.]

Neuroglia, the non-neuronal cellular components of the central nervous system, is a word based upon a Greek term meaning sticking together or glue. Cognate words include glioma, gliosis, and glioblastosis.

— STANLEY M. ARONSON, MD



RHODE ISLAND DEPARTMENT OF HEALTH  
DAVID GIFFORD, MD, MPH  
DIRECTOR OF HEALTH

## VITAL STATISTICS

EDITED BY COLLEEN FONTANA, STATE REGISTRAR

### Rhode Island Monthly Vital Statistics Report Provisional Occurrence Data from the Division of Vital Records

Underlying Cause of Death	Reporting Period			
	January 2006	12 Months Ending with January 2006		
	Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	203	2,848	266.2	4511.0
Malignant Neoplasms	194	2,312	216.1	6,331.5**
Cerebrovascular Diseases	35	474	44.3	702.5
Injuries (Accidents/Suicide/Homicide)	26	421	39.4	6,262.0
COPD	62	522	48.8	467.5

Vital Events	Reporting Period		
	JuLY 2006	12 Months Ending with JuLY 2006	
	Number	Number	Rates
Live Births	1,278	13,089	12.2*
Deaths	822	9,759	9.1*
Infant Deaths	(7)	(97)	7.4#
Neonatal Deaths	(4)	(76)	5.8#
Marriages	928	7,171	6.7*
Divorces	265	3,114	2.9*
Induced Terminations	392	4,775	364.8#
Spontaneous Fetal Deaths	43	994	75.9#
Under 20 weeks gestation	(41)	(941)	71.9#
20+ weeks gestation	(2)	(53)	4.0#

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.

(b) Rates per 100,000 estimated population of 1,069,725

(c) Years of Potential Life Lost (YPLL)

*Note: Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.*

\* Rates per 1,000 estimated population

# Rates per 1,000 live births

\*\* Excludes 1 death of unknown age



## A Breakdown in Communication A Cause of Claims

John Tickner, CPCU, President, Babcock & Helliwell

A breakdown in doctor-patient communication fuels distrust and pent-up anger. The consequences are well documented, and include patient dissatisfaction and diminished quality of care. In addition, according to a study in the *Journal of the American Medical Association*,\* poor physician-patient communication can trigger a chain of events that often leads to a malpractice claim.

Doctors are trained to deal with illness; until recently, few had training in communication skills. But developing good communication is not as complicated as you might think. Making your patients feel listened to and understood is the key.

In a clinical setting, it's easy to forget the human needs of a patient, and just concentrate on his or her medical needs. The patient's first impressions of the doctor and staff members are vital. When you first meet a patient, or a patient's family, introduce yourself by name. Make eye contact. Shake hands to make physical contact, and ask how the patient wishes to be addressed (Mr., Miss, Ms., Mrs., or a first name).

Project a caring attitude and relate to the patient as a person, not just as a clinical condition. Sincere empathy and an understanding of the patient's concerns help instill confidence in you, and will reduce the likelihood of a complaint, should things go wrong.

When talking with patients, use medically correct wording, but avoid medical terminology. Ask your patients if they understand all that's been said. Use open-ended questions, and give them time to answer. Don't give the impression that you're in a hurry. Listen carefully to what patients say and respond therapeutically.

If a patient asks a question, repeat it to make sure that you understand. Encourage the patient verbally and non-verbally – nod your head and say something like "I see, go on." Stay focused on the patient; don't let your mind wander during the conversation. You may continue to work, but make it clear that you're listening. Don't turn your back on a patient while you're talking, don't interrupt a patient who's speaking, and – except in the case of emergencies – instruct your staff not to interrupt you while you're with a patient.

At the end of a visit, it's important to repeat what you've told the patient by summarizing key points. If you must deliver bad news, don't make it sound better than it is.

Ask the patient if he or she has any additional questions. Resolve complaints and misunderstandings about care or other matters now, before any resentment builds.

Finally, if appropriate, thoroughly explain your diagnosis, treatment plans, and options. Research has shown that involving a patient in the development of a treatment plan can lead to better compliance and an improved outcome. However, if a patient refuses to follow your plan, experts recommend that you accept that decision without judgment or criticism. (It's important that you document this refusal in the patient's file.) Tell the patient to call you with any further questions, and make sure he or she knows how to reach you.

Two other points: 1) Be courteous to relatives, and be willing to answer general questions about the patient's condition without compromising confidentiality. 2) Respect patient confidentiality, even in social situations, and instruct your staff on the importance of confidentiality in all settings.

Effective doctor-patient communication helps the patient to understand his or her illness, enhances patient satisfaction, and – many claim – actually assists in the healing process. In addition, good doctor-patient communication is the single most effective claims-prevention measure. It can reduce malpractice litigation, saving you time and expenses in the long run.

\* Levinson, W., "Physician-patient communication: the relationship with malpractice claims among primary care physicians and surgeons" *JAMA* 277(7): 553-59, February 19, 1997.

*John Tickner, CPCU, is president of Babcock & Helliwell, a privately held independent insurance agency established in 1892 that provides professional insurance-related services of all kinds. Babcock & Helliwell is an agency for ProMutual Group, New England's largest medical malpractice insurance provider and the second-largest provider in Rhode Island.*

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# THE RHODE ISLAND MEDICAL JOURNAL

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## NINETY YEARS AGO, JANUARY 1917

Frank F. Peckham, MD, in "Lateral Curvature of the Spine – An Original Method of Treatment," discussed physiological and mechanical treatments; e.g., permanent jackets.

Harry S. Bernstein, MD, in "Initial Experiences in the Office of the State Pathologist," described advances made in this new office, created by the state legislature in 1914. For instance, the staff initiated postage-delivery of specimens: "a 5 cents stamp covers the postage of a specimen of sputum in its appropriate container." The state collected specimens three times daily from a post office box. Data from the office included 126 stool specimens examined for typhoid bacillus in the past 2 years; 4 tested positive (2 on different occasions from the same person). In the first year, the laboratory analyzed 99 specimens for diagnosis of malaria; 6 were positive.

William L. Harris, MD, in "Pelvic Appendix," cautioned: "...a ruptured, post-colic appendix, or a gangrenous appendix within the true pelvis, frequently yields no physical signs whatever."

An Editorial, "Campaign Against Wood Alcohol," urged readers: "See to it that your barber uses only the best toilet articles, and that the ginger ale you drink is one that does not contain this poison."

## FIFTY YEARS AGO, JANUARY 1957

Merrill C. Sosman, MD, Samuel A. Levine, MD, and J. Engelbert Dunphy, MD, all faculty at the Harvard Medical School, had presented a panel discussion "A Brigham X-Ray Conference: Medical and Surgical Cases," at the [October 1956] Interim Meeting of the RI Medical Society. The Journal reprinted the discussion.

Michael G. Pierick, MD, and Taras Hanusheusky, MD, contributed "Chronic Arterial Insufficiency and Fatal Anaphylactoid Transfusion Reaction." A 15 year –old girl, who had had ankylosing rheumatoid arthritis for the previous 5 years, was admitted to Our Lady of Fatima Hospital for rehabilitation. Several years of adrenal steroids had relieved her pain, but left her with knee deformities, moon facies, lethargy, and "depressive type of personality change." She moved from bed to wheelchair. The treatment goal was to increase her mobility. After 3 weeks of a gradual decrease in prednisone, she had no ill effects; she lost 12 pounds; and her spirits improved. On the 14<sup>th</sup> day after the end of all cortisone therapy, she received a supportive whole blood transfusion of 500cc of Group A,, RH+ blood. The patient died of a pulmonary edema, eight hours after the onset of the reaction.

## TWENTY-FIVE YEARS AGO, JANUARY 1982

Charles E. Millard, MD, in President's Corner, contributed "Health Planning May Be Dangerous to Your Health." He objected to proposals to reduce the number of hospitals and nursing homes, in light of the high occupancy rates for those institutions in RI.

An Editorial, by Seebert J. Goldowsky, MD, "Nursing Home Bed Information System," praised the recent bed clearinghouse in Rhode Island, organized by the Hospital Association of RI, the RI Medical Society, the RI Professional Standards Review Organization, the State Department of Social and Rehabilitative Services, and the State Department of Health.

Toussaint A. Leclerq, MD, FACS, contributed "Epidural Stimulation for Pain Control in the Failed Disc Syndrome." He noted: "Success is possible in half of the cases if carefully selected."

Constantine P. Pagonis, MD, and Paul C. Hessler, MD, in "Recurrent Pacemaker Electrode Displacement in The Right Atrium With Capture," noted: "Improved leads reduce the prevalence of this complication."

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## Columns Key

AP	Advances in Pharmacology
HBN	Health by Numbers
HIU	Health Insurance Update
Image	Image in Medicine
JD	Judicial Diagnosis
PHB	Public Health Briefing
PL	Physician's Lexicon
QP	Quality Partners

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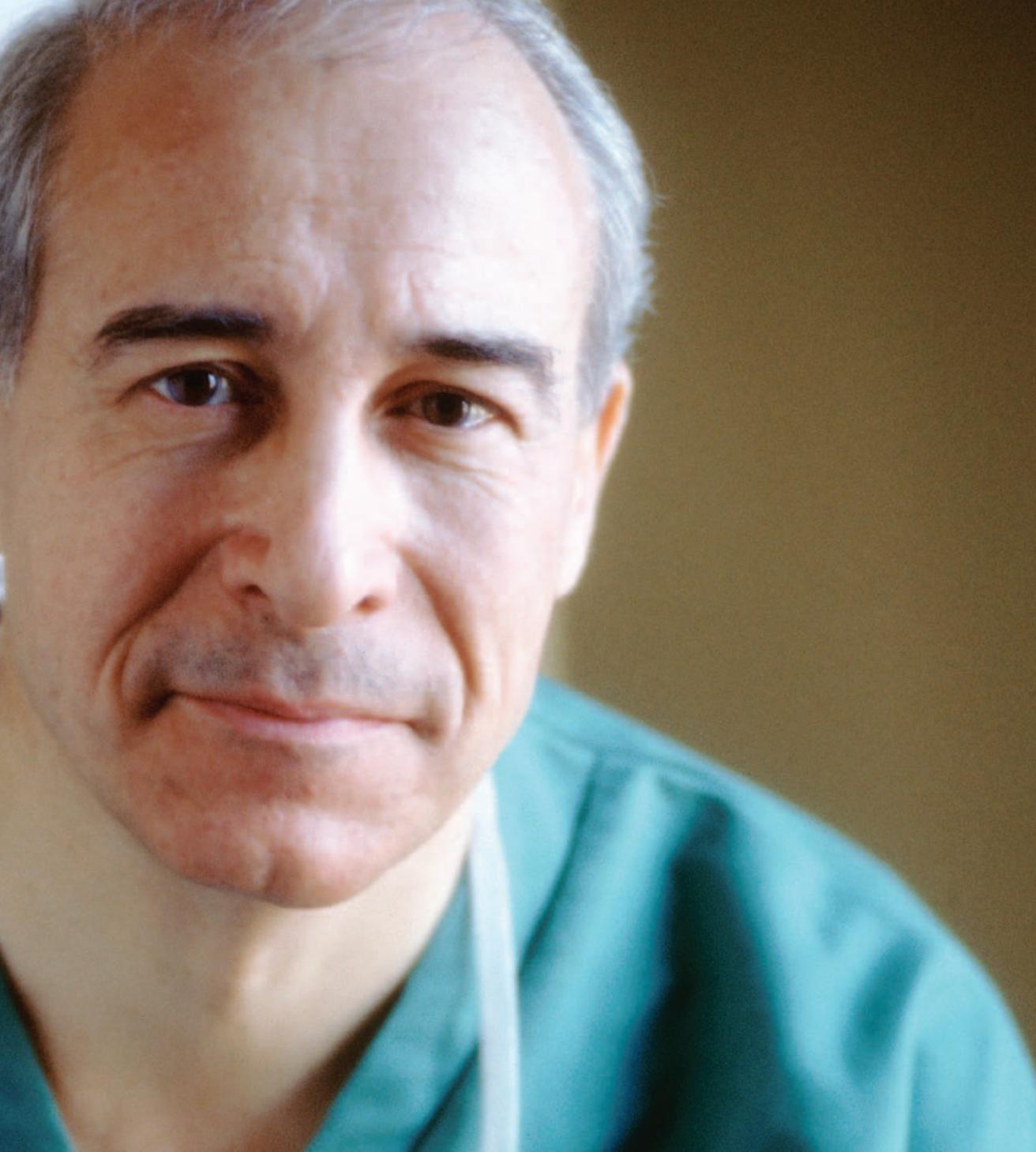
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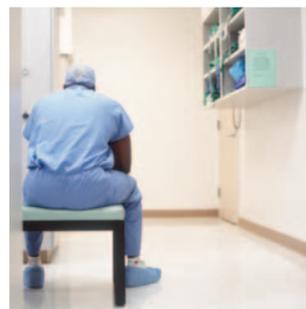
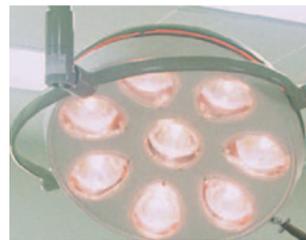
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