QUALITY OF FUNCTIONAL RETURN IN LIMBS AND TISSUES REPLANTED AND--ETC(U)

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# Quality of Functional Return in Limbs and Tissues

Replanted and Transplanted by Microsurgical Techniques

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**ABSTRACT:**
This report covers the experimental background, instrumentation and equipment necessary to perform successful microvascular replantation or transplantation of composite tissue. Various experimental animal models used to evaluate microsuture material, technique, and the effect of vasoplastic drugs are discussed. The experimental uses and clinical applications of autogenous microvascular grafting, microsurgery, and microvascular anastomotic technique are discussed. Clinical applications and functional results of microvascular transplants of neurovascular island flaps, muscles, digits and toes are included.
Dedicated to Mr. Jay Framan
Chief Scientist, Office of Naval Research, San Francisco, California

For his invaluable advice and counsel throughout the duration of this grant
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We are indebted to the Ralph K. Davies Medical Center for its constant help and support of the Microsurgical Research Laboratory and to Dr. Norman Chater for initiating the laboratory and serving faithfully as its Director.

We are particularly in debt to Miss Hilda Thums, who has managed the books, reports and paperwork associated with this grant over the past four years, and finally to Miss Linda Groshell for her help in preparing this final report.
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SUMMARY OF RESEARCH ACCOMPLISHED

Functional recovery after microsurgical replantation and transplantation is dependant upon the successful restoration of circulation within a critical period of time, followed by motor and sensory regeneration. This research project has been directed towards evaluating and stabilizing the many variables that come to play in the execution of a successful experimental or clinical replant or transplant. The organization of the project may be summarized as follows:


II. Microsurgical instrumentation, the modification and improvements of such instrumentation and the microsurgical laboratory. References: 19, 40, 56, 70.

III. Execution, evaluation and preservation of a fail-safe microvascular anastomosis and a micronerve repair. References: 7, 8, 12, 16, 20, 22, 34, 55, 57, 70, 97.

IV. The replacement or elongation of the neurovascular pedicle. References: 23, 41, 60, 62.

V. The control of vascular spasm, occlusion, and thrombosis. References: 10, 11, 18, 21, 22, 53, 126.

VI. Monitoring of the post-operative circulation. References: 119, 120, 121.

VII. Evaluation of nerve regeneration and function. References: 5, 6, 14, 47.

VIII. Dicemination of experimental and clinical techniques and results. References: 1, 2, 3, 14, 17, 38, 39, 43, 45, 48, 49, 50, 51, 52, 54, 59, 61, 93, 94, 95, 96, 97, 125.

IX. Personnel involved in the project and their contributions.

X. Financial statement of support, income and expenditures.
I. SELECTION OF RESEARCH AND CLINICAL MODELS

One of the early primary objectives of the research project was to develop an experimental model to evaluate the transplantation of single muscles from one part of the body to the other on an extended neurovascular pedicle. It was the feeling of the primary investigator that the entire field of muscle transplantation had great potential in the restoration of function after injury, to the upper extremity such as partial or total amputations, destructive injuries with loss of substance, proximal nerve injuries due to gunshot wounds, or traction injuries, involving the brachial plexus. Dr. Leonard Gordon, the first microvascular fellow accepted this challenge and set up a research model in the Rhesus monkey. After considerable dissection he decided on the lateral head of the gastrocnemius muscle as a good unit for transplantation from the lower to the upper extremity. This muscle was to be revascularized and reinnervated with long interpositional nerve and vascular grafts. The unanswered questions at the time were what type of nerve graft should be used, how long should the interpositional grafts be, and how much ischemia can a totally isolated muscle tolerate.

There are potentially two types of nerve grafts that can be used, one is a fresh graft and the other a pre-degenerated graft. There have been some comments in the literature that pre-degenerated grafts may be better grafts, but no experimental work has been done to substantiate this clinical observation. Accordingly, Dr. Gordon set up an experimental model in the rat (Ref. 44) in which he inserted fresh autografts and pre-degenerated grafts into fresh defects and pre-cut degenerated defects. The results of this experiment were documented by axion counts distal to the anastomosis and strain gauge studies of the return of function to the rat muscle. The results of this experiment confirmed that the pre-degenerated grafts performed better when used in previously cut defects and fresh cut grafts were better when used in fresh cut or acute defects.

The next question was how long an ischemia time could a totally isolated muscle tolerate without irreversible changes. To establish this, another model was set up in the rat in which an isolated muscle group was studied for various periods of ischemia by clamping the artery, the vein and both the artery and vein. Many reports are available in the literature regarding ischemia time after tourniquet, etc., but no reports could be found on isolated muscle ischemia. The results of this experiment were evaluated by histological sections of the muscle and electron microscopy studies of the muscle. The conclusions were that after one hour of total ischemia, be it either the artery, vein, or both, the muscle demonstrated irreversible changes. Armed with this information, the Rhesus monkey muscle transplant was set-up using the lateral head of the gastrocnemius and a fresh autogenous nerve graft of the sural nerve of the leg, extending from the ankle to the posterior thigh. The muscle was then transplanted to the forearm and reinnervating it with a nerve graft from the elbow up to the scapular region anastomosing the nerve to the gastrocnemius and the sural nerve to a branch of the dorsal scapular nerve. The muscle was revascularized with a long A.V. pedicle utilizing the radial artery and vein from the wrist up to the cubital fossa (Ref. 46).

Six transplants were performed with considerable difficulty working in the laboratory of Dr. Ralston, in the Anatomy Department of the University of California. These animals were then caged and followed for six months at which time they were re-anesthetized and the animals muscle set up at a strain gauge, the proximal interpositional nerve graft isolated and the nerve stimulated and the
strength of contraction recorded. In four out of the six muscle transplants, evidence of good muscle reinnervation and function and strength were recorded. In one transplant the nerve graft could not be located and in the last transplant it was felt that the muscle failed to survive because of a vascular compromise, rather than failure of nerve regeneration. The results of these early studies established the principle that tissue could be transplanted from one part of the body to the other with microneurovascular techniques with survival and reinnervation of function. Although the model involved a muscle, it was felt that the same principal could be applied to composite skin, with or without the underlying bone. Additional studies were performed in the primate using pre-degenerated grafts and fresh cut grafts performed in the rat (Ref. 34). This study has been completed, the axon count performed (Ref.127).

The problem of replacing long segmental defects of bone has plagued the orthopedic and reconstructive surgeon throughout history. The ordinary bone graft is a devascularized structure serving only as a scaffold for the substitution of living bone. It was the principal investigators feeling that a vascularized bone graft could be used to replace the segmental defects clinically, and that these vascularized grafts would heal like fractures being nourished by a good blood supply on either side of the bone junction.

The rib cage has traditionally been a donor area for bone grafts. An experimental model was set up in the dog to determine first whether the rib could survive as a fresh graft on it's intercostal blood supply and secondly, to determine whether the intercostal blood supply must come from the nutrient artery to the rib which enters it far posteriorly or from the periosteal supply to the rib which is continuous and segmental from the intercostal neurovascular bundle. The dog rib model was used with Dr. Phillip Hendel setting up and performing the experiment through the Department of Orthopedics at the University of California in San Francisco. The results of the experiment were recorded and documented with tetracycline labeling and technisium scans of the replanted ribs. The results of this experiment established the fact that the vascularized rib could be carried on the intercostal neurovascular pedicle without the posterior nutrient arterial blood supply. The periosteal supply, be it posterior or anterior, is sufficient to sustain the rib graft as a vascularized graft. This information was considered to be significant since the harvesting of a vascularized rib graft is considerably simplified if the posterior nutrient vessel does not have to be included. The results of this experiment have been carried into the clinical field with repeated applications (Ref.13) One of the problems with a vascularized rib graft is that the structure is curved and therefore not suitable for straight linear defects. Another model that was set-up in the dog utilizing the rib straightened with an intramedullary K-wire (Ref.132). The model will also be used as a technique for building articulated parts using the rib covered with split thickness skin grafts and neurovascular island flaps (Ref.126).

The composite microneurovascular island flap is now well established. Studies were still needed to evaluate the control of edema in such composite island flaps, the ischemic time such flaps could tolerate and the amount of traction that their vascular pedicles could tolerate. A model was set-up using the rat foot isolated on the femoral vessels and anterior tibial artery and vein down to the ankle. The isolated foot could then be transplanted to the dorsum of the hind quarters of the animal. With a restrictive collar the animals were prevented from canablizing such transplants and survival could then be evaluated objectively.
The isolated neurovascular pedicle was anastomosed and the effects of various drugs evaluated on the control of edema. This work was summarized in report Ref.79.

The same model was used to study the tolerance of ischemia. The vascular pedicle of the transplanted foot was clamped for increasing periods of ischemia, then the revascularized transplant was treated with steroids and Isoxsuprine to see if the period of irreversible ischemia could be extended. In a control model, it was found that an ischemia period of over six hours was followed routinely by total failure of the transplant. However, if the models were treated with steroids or Isoxsuprine, this period of ischemia could be extended with salvage for several more hours(Ref.138).

Problems with traction on the neurovascular pedicle are a constant problem in clinical surgery in the field of traumatic amputations, avulsions, and in the transplantation of neurovascular compound flaps. An anastomosed pedicle may normally or inadvertently be placed under considerable tension in the process of mobilization or in a post operative setting. Accordingly, a model was set-up to evaluate the tensile strength of an anastomosed vascular pedicle. It was found that in a one millimeter vessel, six to eight sutures re-established the normal tensile strength to the structure and a greater or lesser number of sutures decreases the tensile strength of the repair. This is summarized in report number 55.

A smaller model of the same flap which totally survives routinely was used to study other drugs. If half the abdomen is mobilized on the neurovascular pedicle the entire flap survives routinely. If this vascular pedicle is then transected and repaired, with 140 micron needles, which are relatively large for one millimeter vessels, there is an 80 percent failure rate. With such a controlled failure rate, drugs can then be administered in an attempt to improve survival rate. Such a model was used to evaluate the effects of hydroxychloroquine(Ref.22), and calcium disodiumemetatate(Ref. 25).

The same model was used to study the effects of A.V. reversal on flap survival. In this study the artery was repaired to the vein and the vein repaired to the artery. As might be expected, such a reversal was followed by failure either due to valve structure on the venous side or failure of perfusion of the capillary bed. This same model was used to evaluate the effect of arterial overload. Experimentally and clinically, it is not unusual to have a high arterial in-put with a disporportionate low venous drainage. Attempts to evaluate such an arterial overload were set-up in experiment reference 139.

Several models are still under study, directed toward expanding the original muscle transplantation on the extended neurovascular pedicle. One such model in the rabbit is under study evaluating the loss of physiological function of a muscle when half of its nerve supply is shared with an adjacent muscle or a muscle at a distance connected by a long nerve graft. These contralateral muscle transplants innervated by cross-body nerve grafts, we feel, will form the basis for wide clinical applications(Ref.129).

Rat joint transplantations and cat joint homo experiments are also under study with the Department of Orthopedics at the University of California(Ref.124).
Another model using a pre-fabricated myosensory flap, we feel holds great promise for future experimental and clinical applications (Ref.123).

The afore mentioned experimental models have been applied clinically with the reinnervation of an anesthetic area of the sole of the foot by transplantation of a functioning sensory nerve into a non-functioning nerve to the area of anesthesia, leading to successful healing of a trophic ulcer over the fifth metatarsal head (Ref.64). In another case a trophic ulcer over a heel, (Ref.31) healed after a similar nerve transfer. Neurovascular island flaps have been transplanted from the sensory area of the toe to the sensory areas of the thumb, index, and other digits (Ref.37). Neurovascular island flaps have been taken from irreplaceable amputated digits to reconstruct other amputated digits (Ref.42). Neurovascular island flaps from the first web space have been mobilized and transferred to trophic ulcers and irreversibly scarred areas on the sole of the foot (Ref.65), on the dorsum of the foot (Ref.66), and to the pressure area of the heel (Ref.115). Neurovascular island flaps have now been used to resurface below knee amputation stumps which have poor cover and are subjected to breakdown from the prosthesis (Ref. 106.)

The vascularized rib graft has been clinically, with and without a skin island to reconstruct defects of the leg as a result of trauma(Ref.37), congenital pseudoarthrosis (Ref.62 and 63), and in the mandible(Ref.58,59,105).

The successful muscle transplantation in the monkey (Ref.46) has been realized in man to restore function to the upper extremity and facial animation (Ref.116). The concept of using the muscle as a non-functional, merely for cover or in the acute high voltage burn injury are summarized in references 9, 102, 103, 113, 114.
II. MODIFICATION AND IMPROVEMENT OF MICROSURGICAL INSTRUMENTATION AND LABORATORY

The microsurgical laboratory not only provides the environment for experimental study, but also serves as a training ground for physicians, fellows and residents where they can acquire the necessary skill to perform clinical microvascular and microneurovascular anastomosis. The laboratory at the Ralph K. Davies Medical Center has served this dual function for many years and has gained an international reputation in both fields. A skilled microsurgical technician is in charge of the training and also assists in the research projects. Microsurgical fellows, before they can function actively in a research project, or assist in clinical cases, must acquire these skills and dexterity. They are subjected to a concentrated two week course in microsurgical techniques and then are integrated into the various research projects. The results of these projects have led to numerous modifications in the instrumentation and the techniques involved.

The Zeiss operating microscope Model #1, was modified specifically for the investigator by Urbin Engineering Company of Burbank, California, using a special beam splitter to convert a single microscope into a double one. Such a modification has made the double microscope, which is invaluable as a teaching and research tool, available to many laboratories at considerably less expense than the large double microscopes.

Microvascular instrumentation has been modified to increase operating efficiency and dexterity. The standard forceps available have been elongated to more easily fit into the first web space and converted from the flat surface to a round surface by applying silicone covering. Such instruments can then be rotated with ease under the microscope permitting a wider range and dexterity. Microvascular clamps have also been modified to prevent vascular damage. Studies from our laboratory have demonstrated that clamps of more than 30 grams per square millimeters produce endothelial damage. A new technique of repairing vessels leads to the modification of the clamps permitting the back wall to be sutures first (Ref. 83).

One of the principal problems in operating with a microscope in a clinical setting is getting the microscope into position with relation to the operator and patient. This led to the design of a Universal operating table by Dr. Leonard Gordon, in which the patient's extremity, head or trunk is placed in a trough permitting the operators to position themselves on either side in a comfortable efficient manner. (Ref. 40)

These various experimental models and equipment, modifications and instrumentation have been outlined and described in references 19, 36, 70, 76, 56.

The laboratory at the Ralph K. Davies Medical Center has served as a model throughout the United States and the world for other microsurgical laboratories, utilizing the instrumentation, set-up, tables, etc. None of these instrument modifications or microscope modifications have been patented by the laboratory or the principal investigator.
III. EXECUTION, EVALUATION AND PRESERVATION OF A FAIL-SAFE MICROSURGICAL ANASTOMOSIS AND NERVE REPAIR

It goes without saying that a microvascular transplant in order to be successful must have a patent repair. In the laboratory these microvascular repairs have been studied extensively, with scanning electron microscopy to evaluate the degree of endothelial trauma, endothelial regeneration, type of cell present, acutely and chronically at the anastomosis site, the effects of various types of needles and suture material, and the degree of local trauma, etc. (Ref. 22, 24, 57)

It was also noted that in the experimental animal, aneurysms were common at the site of the anastomosis. These have been completely eliminated by an experimental cuffing technique which has been transferred immediately to the clinical field (Ref. 7) with autogenous vein graft cuffing of all clinical anastomosis (Ref. 7, 20, 22).

As stated previously, the number of sutures necessary to perform a vascular repair with normal tensile strength is summarized in Ref. 55.

The effect of local hematomas about the site of vascular repairs has long been implicated as a cause for secondary thrombosis. This was evaluated in study # 34, and found not to be statistically valid. The challenges of clinical microvascular repairs have led to the development of a technique in which the posterior sutures are placed first, working anteriorly around the vessel. In this fashion the lumen is continually visualized preventing the placing of sutures between the anterior and posterior wall. Rotation of the vessel is also unnecessary, a real consideration in difficult situations where room is not available. (Ref. 16) This technique has been facilitated by the tilted microvascular clamp previously mentioned in section I. (Ref. 83)

Considerable clinical interest has been shown recently in an end-to-side over end-to-end repair. The patency of these two types of repair has been evaluated in the experimental model (Ref. 12). With good technique, end-to-side repairs have as high a patency rate as an end-to-end repair. It was also noted in histological studies of these various repairs that the wall of the vessel at the side of the repair showed differential hypertrophy. Studies of the cause of this hypertrophy and it's relationship to the direction of flow are outlined in reference #131.

The evaluation of vascular patency on a clinical experimental basis is usually confirmed by a "milking test" to demonstrate the filling of the vessel before and after the anastomosis. There's some question whether this test produces endothelial trauma and possibly secondary thrombosis. This was studied in reference # 24. Scanning electron microscopy pictures of the vessel wall failed to reveal excessive endothelial trauma produced by this clinical test.

Control of bleeding at the microvascular repair has been eliminated by the use of the microvascular autogenous cuff as mentioned earlier. This can also be controlled with various topical agents such as Avetine, a strong thrombogenic substance. This work was summarized in reference 84.
The actual step by step microvascular technique is detailed and summarized in several publications, # 70, 76, 100, 56, 19, 87. These techniques have also been recorded on TV tapes for The American Society of Plastic and Reconstructive Surgeons (Ref. 96), and the American Society for Surgery of the Hand (Ref. 100).
As stated in Section I, the primary thrust of this investigation has been to try to transplant or replant composite tissue on an elongated neurovascular pedicle. A careful study of different types of autogenous and homogenous and prosthetic materials has been tried. The relationship between vessel graft size of the donor and recipient, and the interpositional graft has been summarized in Beuchler's work (Ref. 60). This work also carefully evaluates the different types of autogenous and heterogenous grafts available. Preserved umbilical arteries from placentas have been used as interpositional arterial grafts (Ref. 71). A wide variety of prosthetic grafts are used in macrovascular surgery but few are adaptable to microvascular surgery. As a matter of fact, synthetic grafts of one millimeter in external diameter thrombose routinely (Ref. 23 and 26).

The results of these successful experimental procedures in animals have established the microvascular interpositional autogenous vein graft. Such grafts are used extensively on a clinical basis now and our experience has been summarized in reference 78, and specifically for replacement in severe crushing injuries in reference 41, and in extensive avulsive injuries such as the scalp in reference 68, and as part of the replantation and transplantation routine in references 4 and 34.
V. CONTROL OF VASCULAR SPASM AND PLATELET AGGLUTINATION AND THROMBOSIS

The control of vascular spasm in small vessel anastomosis is second only to the technical problems associated with creating a functional anastomosis. In large vessel repairs with high pressure and volume of flow, vascular spasms is seldom a problem. With small vessel repairs, vascular spasm can produce total occlusion. Slight variations in viscosity, pressure and flow rates become critical. Arterial blood pressure can be maintained by keeping a high blood volume, viscosity can be reduced by hemodilution and platelet agglutination reduced by pre-treatment with Aspirin and low molecular weight Dextran. The clotting process itself can be inhibited with Heparin and other anti-coagulants which carry with them the danger of post-operative bleeding and hematomas. The efforts of our laboratory under this grant have been directed toward the control of vascular spasms with various vasoplectic agents which affect the vessels either directly or through their alpha blocking properties or Beta adrenergic properties. The variety of drugs in these various categories have been tested in the rat model in the delayed and acute flap by Dr. Philip Hendel. Variations in circulation in these models have been documented and evaluated by Xenon washout studies (Ref.10 and 11).

Ioxsupsrime has been demonstrated repeatedly to enhance flap survival by its direct muscle relaxing effect and its adrenergic effect. This has been further elaborated upon in our laboratory utilizing the rat abdominal flap model of Finseth and Xenon washout studies (Ref.18). The pre-treatment time necessary to achieve maximum effect of this drug has also been worked out, using the same model which experimentally appears to be about five days (Ref.53).

The effect of Ioxsupsrime given interarterially has been studied (Ref.118). This vasodilator affect on the capillary bed has been documented with micro-arteriographs reported in reference 29. Other drugs which have no measurable affect on the control of microvascular spasm are Calcium Disodiumedetate (Ref.25), Hydroxychloroquine (Ref.73), and Thrombolysin (Ref.142). A new vasoplectic agent, Minipres, is now under study (Ref.141). These experimental findings have been used clinically for many months with elective pre-treatment with Ioxsupsrime and the pre-operative, intra-operative, and post-operative use of Aspirin, low molecular weight Dextran and in acute crushing replants, Heparin.

When replants or transplants develop post-operative thrombosis, requiring re-operation, the patient is again placed on the same routine with the addition of Heparin. Intra-operative Thrombolycin has been used on several occasions with variable results. Although it is difficult to come up with statistically valid data, it is our present impression that pre-treatment with Ioxsupsrime does prevent the vascular spasm seen in the immediate post-operative as well as the intra-operative setting. The vasospastic effect of nicotine has been well documented with the loss of a successful replant, in three patients who began smoking in the immediate post-operative period (Ref.21).
VI. MONITORING OF POST OPERATIVE CIRCULATION

Circulation to a microvascular replant or transplant can be documented clinically by the evidence of capillary return, tissue turgor, temperature and color. The standard instruments available to augment these clinical observations, such as Doppler probes, thermisters, photoelectric plethesmographs have been used for some time. However, there are many situations in the clinical post operative scene where none of these instruments are of value. This is particularly true in the transplantation or replantation of large blocks of tissue or pure muscle tissue covered with a skin graft. In these instances, what is direly needed is a micro-implantable monitor to read out flow in these small vessels, oxygen tension or deep tissue temperature. We are still pursuing these avenues of research and have made some progress with micro fiberoptic implantable probes (Ref.120), cutaneous post operative oxygen tension monitors (Ref.119), and miniaturized plethesmograph(Ref.135 and 136). The possibility of implanting a micro-Doppler through a 25 gauge needle still seems technically feasible(Ref.135). There is absolutely no doubt that the technology to achieve this type of accurate flow monitoring is available- it is simply a question of adapting this technology to the microvascular transplant and replant.

Techniques for monitoring circulation utilized by this group have been summarized in various clinical publications outlining the replantation routine (Ref. 71 and 22), toe transplantation(Ref.14), scalp replantation (Ref.68).

One clinical method recently devised is to remove the nail of a replant and document the bleeding from the nail bed in the immediate post operative period. This technique has also been found to decrease venous congestion in replants where the venous anastomosis has been difficult because of the small size of vessels in the distal replant or complications with the venous anastomosis post operatively, or situations where only an artery can be repaired.
VII. EVALUATION OF NERVE REGENERATION AND FUNCTION

The return of function to muscles replanted on extended neurovascular pedicles is well documented in Gordon's experimental model previously discussed and described in reference 46. Over the past several years a large volume of clinical material has now become available and the functional results in the clinical transplants and replants have been reported in detail involving gait analysis, sensory return, two point touch, proprioception, etc. (Ref. 1, 91, 14) Specific studies on the neurovascular island transplant from the toe to the hand have been evaluated in references 47 and 5). The return of sensation in nerve transplants as previously mentioned are documented in references 31, 64.

Evaluation of sensory and motor return after microsurgical nerve grafting to the brachial plexus, upper and lower extremities are documented in references 71, 6, 107. A detailed clinical study by Goodstein in reference 80, correlates the results of groin flap transplants with the microvascular hook-up. A computerized program for replants and transplants has been set-up in study reference 128. A detailed evaluation of the results after single digit replants is presented in reference 3. The entire volume of clinical material, digit and limb replants, toe transplants, neurovascular island flaps, nerve and muscle transplants, is being analyzed for presentation at a Symposium set up by the American Academy of Orthopedic Surgeons to compare the results from various centers around the country in June 1981. These reports are numbered 109, 110, 111, and 112.
VIII. DISSEMINATION OF EXPERIMENTAL AND CLINICAL TECHNIQUES AND RESULTS

Experience gained in the experimental microsurgical laboratory and in the numerous clinical cases performed by the microsurgical transplantation and replantation service at the Ralph K. Davies Medical Center have been summarized in numerous presentations, publications, etc. A general view of the application of microsurgical techniques was outlined at the meeting of International Plastic and Reconstructive Surgeons in Rio in 1976, and appears in their transactions of this meeting (Ref. 86). Similar reviews were presented at the Swedish Symposium of Microsurgery (Ref. 1), and at the Hospital for Special Surgery in New York (Ref. 2). The techniques developed in this institution for replants have been carefully outlined in references 4, 67, 104, 96, 58, 61, and 85. The role of microsurgery in hand surgery, digital transplantation, and composite tissue transplantation to the hand for reconstruction have been outlined in references 51, 32, 77, 17, 52. The role of techniques utilizing microsurgical procedures have been outlined in references 50, 69, 38. Microsurgical transplants to the lower extremity of skin, bone, or osteocutaneous flaps for cover of the difficult wound, chronic osteomyelitis, and amputation stumps have been outlined in references 39, 43, 48, 45, 63, 59, 54, 93. The value of microsurgical transplants and replants in the field of aesthetic surgery are outlined in references 85, 63, 89. Laboratory techniques, instrumentation and their application have been assembled in an exhibit which has received first prize and honorary mention from the American Society of Plastic and Reconstructive Surgeons, the American College of Surgeons, and several local and distant Society meetings (Ref. 94). A detailed elaborate 35 millimeter slide library and educational file are available at the Ralph K. Davies Medical Center office (Ref. 94).

Educational tapes on these clinical and laboratory techniques have been prepared for the Educational Foundation of the American Society of Plastic and Reconstructive Surgery (Ref. 110), for the American Society for Surgery of the Hand (Ref. 97). An extensive series of educational tapes and a movie are under preparation for a Symposium to be given in June of this year (Ref. 125).
IX. PERSONNEL

The following individuals have participated in this project:

Harry J. Buncke, M.D.
Principal Investigator, and participant in all projects.
Clinical Professor, Division of Plastic Surgery, University of California, San Francisco, and
Chief, Ralph K. Davies Medical Center Replantation and Transplantation Team.

Norman L. Chater, M.D.
Professor of Clinical Surgery, Department of Neurosurgery, University of California Medical School, San Francisco, and
Director, Microsurgical Laboratory at the Ralph K. Davies Medical Center,
Participated on projects (Ref. 38, 71, 114)

Philip Weinstein, M.D.
Associate Professor and Chief, Section of Neurosurgery, Department of Surgery,
University of Arizona Medical Center
Participated on studies (Ref. 57, 124)

Frederick Finseth, M.D.
Assistant Clinical Professor, Division of Plastic Surgery, University of California Medical School, San Francisco, and
Member, Microsurgical Transplantation and Replantation Team of the Ralph K. Davies Medical Center. January 1979 through September 1980
Participated on studies (Ref. 7, 20, 22, 16, 5, 29, 21, 19, 67, 122, 138, 19, 143, 99.)

Juan J. Rodrigo, M.D.
Assistant Professor, Department of Orthopedic Surgery, University of California, San Francisco.
Participated in projects (Ref. 13 and 124)

Norman K. Poppen, M.D.
Assistant Professor, Department of Orthopedics, University of California, Davis School of Medicine.
Participated in projects (Ref. 82, 5, 30, 21)

Tom R. Norris, M.D.
Attending Orthopedic Surgeon and Hand Surgeon, Presbyterian Hospital, San Francisco.
Participated in projects (Ref. 82, 5, 30, 21)

Zoltan Szabo
Chief Technician, Microsurgical Laboratory, Ralph K. Davies Medical Center through June 1980.
Participated in most of the research projects and particularly in the S.E.M. studies (Ref. 57)

Mark Phillips
Chief Technician, Microsurgical Laboratory, Ralph K. Davies Medical Center Microsurgical Laboratory, 1980 to present.
Participated in all recent projects and is active in the on-going microsurgical teaching program.
MICROSURGICAL FELLOWS

Leonard Gordon, M.D.
June 1975 through June 1976
Contributions: (Ref. 36, 39, 40, 44, 46)
Covered in Progress reports 0001AB, AC, AE

Bernard S. Alpert, M.D.
June through December 1976
Contributions: (Ref. 4, 23, 38, 41, 42, 78, 89)
Covered in Progress reports 0001AB, AC, AE

Ueli Beuchler, M.D.
June through December 1976
Contribution: (Ref. 60)
Covered in Progress report 0001AB, AC.

Max Mehdorn, M.D.
Contributions: (Ref. 70 and 71)
Covered in Progress report 0001AF

K.G. Shah, M.D.
January through June 1977
Contributions: (Ref. 25, 49, 52, 73, 78)
Progress report 0001AF

Stephen Mathes, M.D. (Assoc. Prof. of Surgery, Division of Plast. & Reconst. Surg.)
University of California, San Francisco
Contribution: (Ref. 84)

Elliot Rose, M.D.
July through December 1977
Contributions: (Ref. 47, 75, 128, 130)
Progress report 0001AG

Harold Mac Donald, M.D.
July through December 1977
Contributions: (Ref. 8 and 129)
Progress report 0001AG

Wallace Goodstein, M.D.
January through June 1978
Contributions: (Ref. 26, 27, 80, 28, 131)
Progress report 0001AJ

Timothy Walker, M.D.
June through December 1978
Contribution: (Ref. 118)
Progress report 0001AJ

Lawrence Colen, M.D.
June through December 1978
Contributions: (Ref. 55, 79, 81)
Progress report 0001AL, AM
MICROSURGICAL FELLOWS CON'T

Carolyn Cline, M.D.
June 1978 through June 1979
Contributions: (Ref. 34, 73, 120)
Progress report 0001AL, AM

Phillip Hendel, M.D.
January 1979 through October 1979
Contributions: (Ref. 10, 11, 13, 18, 30, 86, 133, 134)
Progress report 0001AM, AN.

Barry Zide, M.D.
January through June 1979
Contributions: (Ref. 53, 85, 88)
Progress report 0001AN

Gerald D. Harris, M.D.
June through December 1979
Contributions: (Ref. 16, 54, 21, 7, 20, 22, 126, 137, 17, 86, 33)
Progress report 0001AP, AQ

John Schimmel, M.D.
October through December 1979
Contributions: (Ref. 67, 138)
Progress report 0001AQ

Kevin Hagan, M.D.
January through June 1980
Contributions: (Ref. 139, 9, 63, 123, 106)
Progress report 0001AQ, AR

Elizabeth J. Hall, M.D.
January through June 1980
Contributions: (Ref. 3, 6, 12, 31, 124, 107)
Progress report 0001AQ, AR

Roxanne Johnson-Giebink, M.D.
June through December 1980
Contributions: (Ref. 4, 99, 141)
Progress report 0001AS

R. Thomas Grotz, M.D.
June through December 1980
Contributions: (Ref. 24, 119, 99, 95)
Progress report 0001AS
Financial Statement
1976 through 1980

1976- Monies received
  Navy Grant - 10,000.00
  Transfer from
  savings account ----- 10,746.37
  Assistant fees - 1,700.00
  Crosby Grant - 5,000.00
Total 27,446.37

Expenses; $23,463.72

1977- Monies received
  Navy Grant - 20,000.00
  Assistant fees - 5,888.15
Total 25,888.15

(plus cash on hand) 5,629.42

Expenses; 28,008.00

1978- Monies received
  Navy Grant - 20,000.00
  Hearst Grant - 25,000.00
  Transfer from
  savings account ----- 2,500.00
  Assistant fees - 22,769.44
Total 70,269.44

(plus cash on hand) 3,509.50

Expenses 40,574.41

1979- Monies received
  Navy Grant - 13,000.00
  Hearst Grant - 20,000.00
  Assistant fees - 47,281.06
Total 80,281.06

(plus cash on hand) 5,704.60

Expenses 60,942.76

1980- Monies received
  Navy Grant - 10,000.00
  Transfer from
  savings account ----- 42,000.00
  Crosby Grant - 2,500.00
  Mcintosh " - 2,500.00
  Assistant fees - 64,893.00
  Misc. - 7,867.63
Total 129,780.63

Expenses; 105,737.90
**January 1, 1976 - December 31, 1976**

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<thead>
<tr>
<th>Date</th>
<th>Cash on Hand</th>
<th>Deposits</th>
<th>Disbursements</th>
<th>Cash on Hand</th>
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**Disbursements**

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<td>Research Sp.</td>
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<td>Research Expense</td>
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<td>Lab Supplies</td>
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<td>Photo Supplies</td>
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<td>Movie Exp.</td>
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<td>Animal Exp.</td>
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<td>Miscellaneous</td>
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<td>Equipment Purchase</td>
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January 1 - December 31, 1977

Cash on Hand - January 1, 1977 ------------ $5,629.42

Deposits  
Expenses  
Cash on Hand - December 31, 1977 $3,509.57

Expenses

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<td>Loan Repayment</td>
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<td>Microsurgical Fund</td>
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<td>Secretarial Help</td>
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<td>Postage</td>
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<td>Med. Illus. and Photo</td>
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<td>Liability Insurance</td>
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<td>Taxes</td>
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<td>TOTAL</td>
<td>$28,008.00</td>
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January 1, 1978 - December 1, 1978

January 1, 1978
Cash on hand 3,509.50
Deposits 42,769.44

Expenses 40,574.41
Cash on hand, December 31, 1978 5,704.53

Salaries 12,198.30
Tax deposits-payments 5,373.25
RKO Microsurgical Fund 10,000.00
Meetings, Sympos. etc 2,118.00
Books, Educational Material 419.51
Supplies 6,357.91
Instruments 1,537.44
Insurance 2,286.00
Misc. 34.00
Legal fees 250.00

Total Expenses 40,574.41
January 1 - December 31, 1979

<table>
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<td>Total Expenses January 1 - December 31, 1979</td>
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<tr>
<td>Cash on Hand - December 31, 1979</td>
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**Disbursements**

- Animals (lab)                           | 21.00    |
- Repairs                                | 149.80   |
- Equipment Purchases                     | 4,159.39 |
- Microsurgical Fund/Research             | 4,000.00 |
- Special Projects Expenses               | 6,201.94 |
- Expendable Supplies                     | 626.14   |
- Publications Expense                    | 681.40   |
- Salaries                               | 34,455.73|
- Legal Costs                            | 385.00   |
- Tax Deposits                           | 7,297.52 |
- Meeting Expenses                       | 2,137.84 |
- Miscellaneous                          | 827.00   |
**TOTAL**                                | 60,942.76|
### Microsurgical Transplantation Research Foundation

101 N. El Camino Real • San Mateo, California

Telephone 342-8980

<table>
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<th>Account Type</th>
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<td>Withdrawals</td>
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<td>Expenses (see below)</td>
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<td><strong>Cash on hand, December 31, 1980</strong></td>
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**Total:** $44,882.44

### Expenses

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<td>Research space</td>
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<td>Refunds</td>
<td>$8,223.23 (IRS payment in error, withheld FICA refunded to employees)</td>
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</table>

**Total:** $105,737.90
QUALITY OF FUNCTIONAL RETURN TO LIMBS AND
TISSUES REPLANTED AND TRANSPLANTED BY MICROSURGICAL TECHNIQUES

B and C- Index of all technical reports and publications performed under the contract.

PAPERS IN PUBLICATION


26. Use of 1 mm. Gortex Grafts in the Rat Femoral Artery; W. Goodstein, H.J. Buncke, to be submitted.


33. The Role of Microsurgery and Hand Surgery; H.J. Buncke, G.D. Harris.
PUBLISHED PAPERS

34. The Effects of Artificial Postoperative Hematoma on Patency of Microvascular Anastomosis in Rat Femoral Blood Vessels; R. Sadove, C. Cline, H.J. Buncke: Journal of Microsurgery, July-August 1979, pg. 50.


61. Free Toe-to-Hand Transfers; H.J. Buncke: Reconstructive Microsurgery

62. Free Microvascular Rib Transplantation in the Treatment of Congenital
   Pseudoarthrosis of the Tibia: Report of Two Cases; W.R. Murray,
   H.J. Buncke.

63. Treatment of Congenital Pseudoarthrosis of the Tibia with Free

64. Restoration of Sensation to the Sole of the Foot by Nerve Transfer:
   A Case Report; L. Gordon, H.J. Buncke: Journal of Bone and Joint
   Surgery, April 1981.

65. Neurovascular Island Flap from the First Web Space of the Foot for
   Coverage of Plantar Ulcers; H.J. Buncke, L.B. Colen: British Journal
   of Plastic Surgery, 1981.

66. Another Use for the Foot First Web Space Neurovascular Island Flap;

67. Digital Replantation: Current Technique and Practice; J. Schimmel,

68. Successful Replantation of Two Avulsed Scalps by Microvascular
   Anastomoses; H.J. Buncke, E.H. Rose, M.J. Brownstein, N.L. Chater:

69. Revascularization of the Scalp by Microsurgical Techniques After
   Complete Avulsion; N. Chater, H.J. Buncke, and M. Brownstein:

70. Human Umbilical Artery as a Source of Small-Diameter Vascular Grafts;
   H.M. Mehdorn, N.L. Chater, J.J. Townsend, P.R. Weinstein, and H.J. Buncke:
   Graft Materials in Vascular Surgery, Editor, H. Dardik: Year Book Medical

71. Endothelialization of a New Arterial Microvascular Graft Material;
   Mehdorn, H.M., Townsend, J.J., Weinstein, P.R., N.L. Chater, Meyermann, R.,
   1979.

72. Prevention of Thrombosis in Arterial and Venous Microanastomoses by
   Using Topical Agents; W.M. Swartz, R.R. Brink, H.J. Buncke: Plastic and

73. The Effect of Hydroxychloroquine Sulfate in the Prevention of Thrombosis
   at Microvascular Anastomotic Sites; K.G. Shah, C.J. Cline, H.J. Buncke:
   Chirurgia Plastica.

74. The Eely Notes of the San Francisco Microsurgical Symposium. November 6-9,
   1977.

76. Experimental Microsurgical Techniques; M.L. Brownstein, H.J. Buncke, in The Hand, by Tubian. Publisher- W.B. Saunders. (no reprint)

77. Digital Replantation; M.L. Brownstein, H.J. Buncke, in The Hand, by Tubian. Publisher - W.B. Saunders. (no reprint)


81. Increased Tolerance of Ischemia Time by Treatment with the Vasodilator Drug Isoxsuprine; T.N. Wang, L. Colen, F.Finseth, H.J. Buncke: British Association of Plastic Surgeons.(Submitted for presentation at the Bristol-BAPS meeting July 1980.)


84. The Effects of Avatine on Bleeding of Microvascular Anastomoses; L.B.Colen, S.Mathes, H.J. Buncke: Submitted to Annals of Plastic Surgery


89. The Application of Microsurgical Techniques in Aesthetic Surgery; B.S. Alpert, H.J. Buncke: ( no reprint)


94. Exhibit on Microsurgical Replantation and Transplantation by the staff of the Microsurgical Replantation and Transplantation team at the Ralph K. Davies Medical Center: First prize at the Annual Meeting of the American Society of Plastic and Reconstructive Surgeons, San Francisco.

95. The Scope of Microsurgical Replantation and Transplantation, 35 millimeter master slide teaching file, Ralph K. Davies Medical Center.


PAPERS IN PREPARATION


103. The Relief of Venous Congestion in Replanted Digits by Heparinization and Nail Avulsion.


105. The Osteocutaneous Groin Flap Transplanted on the Superficial and Deep Circumflex Iliac Vascular Double Pedicles.


109. Functional Results after Microsurgical Limb Replantation, ibid.

110. Functional Results after Microsurgical Toe Transplantation, ibid.

111. Functional Results after Microsurgical Flap Transplantation, ibid.

112. Functional Results after Muscle Transplantation, ibid.

113. Cover of Large Scalp and Cranial Defects with Latissimus Dorsi Myocutaneous Flap and Simultaneous Bone Grafts.

114. Radical Excision of a Recurrent Sarcoma of the Scalp and Skull with Immediate Reconstruction.

115. The Long Island Flap- The Use of a Neurovascular Island Flap from the Toe as a Sensory Island over the Pressure Area of the Heel.


118. The Use of Intervenous Ioxsuprine to Increase Flap Survival
PROJECTS STILL IN PROGRESS


120. Microfiberoptic Monitoring of Blood Flow in One Millimeter Vessels; C. Cline, H.J. Buncke.

121. Implantable Micro Electrodes for Monitoring Temperature, Flow, and Oxygen Tension; Research staff at the Ralph K.Davies Microsurgical Laboratory.

122. The Evaluation of Muscle Function After Nerve Sharing- A Study in the Rabbit; Research Staff at the Ralph K.Davies Microsurgical Laboratory.

123. The Use of a Pre-Fabricated Musculosensory Flap to Prevent Trophic Ulcers in the Experimental Model in the Rabbit.

124. Homotransplantation of Cat and Rat Joints; Joint project with the Department of Orthopedic Surgery, University of California, San Francisco.


128. Computerized Retrospective Study of Replants and Transplants at the Ralph K.Davies Medical Center.

129. Contralateral Muscle Transplantation with Ipsilateral Cross-Body Nerve Grafting- A Study in the rat and rabbit.

130. Evaluation of Traction Injuries to Neurovascular Pedicles Biomechanical study in the rat.

131. Histological Changes in Vessel Walls Adjacent to End-to-End and End-to-Side Microvascular Repairs.

132. The Use of an Intramedullary K-wire to Straighten Microvascular Rib Transplants.

133. Monitoring of Microvascular Patency with a Polography- A study with the Anesthesia Department of the University of California, San Francisco.
134. The Use of an Implantable Micro-Doppler to Monitor Microvascular Flow—
A Study with Medi-Sonic Instrument Co., and present staff.

135. Miniaturization of a Photo-electric Pylonchosmograph for Monitoring
Microcirculation — A Study with John Comstock, a Bio-Engineer at the
Ralph K. Davies Medical Center, and present staff.

136. Miniaturization of Implantable Thermistors — A Study with John Comstock,
a Bio-Engineer at the Ralph K. Davies Medical Center, and present staff.

137. A Retrospective Clinical Study of the Value of Xenon Washout Technesium
Scans and Hyperbaric Oxygen in the Management of Difficult Replants and
Transplants. Present staff at the Ralph K. Davies Medical Center.

138. The Effects of Steroids on the Salvage of Ischemic Flaps; J. Schimmel
and F. Finseth.

139. The Use of the Abdominal Flap in the Rat — A Study of Arterial Overload;

140. The Clinical Use of a Post Auricular Flap based on the Occipital or
Superficial Temporal Recurrent Arteries.

141. The Value of Miniprier as a Vasodilator in Microvascular Repairs;
R. Johnson-Giebink, H. J. Buncke.

142. The Effects of Thrombolysin On Extending the Ischemia Time of Rat
Flaps; m. Edgerton, and H. J. Buncke.
Conclusion drawn based on this research contract

1. Autogenous composite tissue can be successfully replanted on extended neurovascular pedicles and be followed by the restoration of useful sensory and motor function.

2. Autogenous interpositional micronerve and microvascular grafts are superior to homologous or synthetic grafts, which thrombose routinely in the one millimeter external diameter range.

3. Microvascular instrumentation should be atraumatic, produce minimal endothelial damage and be adapted for ease of manipulation.

4. The ideal microvascular anastomosis should have a minimum of sutures of the appropriate size to reproduce the normal tensile strength of the vessel. Platelet agglutination and clotting are decreased with the use of an autogenous vein cuff around the anastomosis, local and systemic platelet stabilizing drugs, vaso dilation, hemodilution, and adequate arterial pressure.

5. Accurate monitoring of the circulation across the arterial and venous anastomosis is the only absolute method for documenting patency. This is possible in the experimental setting, but not as yet in the clinical setting.

6. Training in microsurgery should follow an organized plan—beginning in the microsurgical laboratory and progressing to the clinical field as basic skills are acquired.

7. Extensive clinical defects can be reconstructed with multiple microvascular transplants of skin, bone, muscle, enervated and vascularized by local nerves and vessels, or distant nerves and vessels ipsilateral or contralateral in origin.
E-Major accomplishments of this research contract

1. The successful functional transplantation of a microneurovascular muscle unit on an extended microneurovascular pedicle within a critical period of ischemia utilizing fresh and predegenerated nerve grafts.

2. Standardization of microsurgical instrumentation, clamps and techniques.

3. Demonstration that microvascular anastomosis of one millimeter in size can be performed successfully in the 99 percentile range.

4. Establishment of an on-going microsurgical research and teaching laboratory which has trained numerous civilian and military surgeons in microsurgical techniques.

5. Demonstration that multiple mutilating injuries can be salvaged with interpositional vessel and nerve grafts taken from expendable donor areas and/or nonreplantable parts.

6. Successful replantation of partial and total scalp avulsions, the successful transplantation of osteocutaneous rib grafts, neurovascular island flaps from the toe to the hand, total toe transplants from the foot to the hand, multiple toe transplants from the foot to the hand, isolated muscle transplants from the leg and trunk to the upper and lower extremity, face and scalp. The successful replantation of single and multiple digits and portions of entire extremities.

7. Dissemination of experimental and clinical microsurgical techniques to the surgical profession.

8. Application of these techniques for the rehabilitation of injured Naval personnel (refer to page 36)
Harry J. Buncke, M.D.
39 N. San Mateo Drive
San Mateo, CA 94401

Dear Doctor Buncke:

This Command is grateful to you for the professional assistance which you rendered during the recent surgery on Chief Deane Rapp. This patient is a highly valued member of the Navy's nuclear submarine program and we appreciate your efforts to help keep this dedicated young man on active duty.

On behalf of Doctor Lichtman and myself, I would again like to thank you for your many contributions to Navy Medicine.

Sincerely,

W. M. LONERGAN
Rear Admiral, MC, U. S. Navy
Commanding Officer
## STUDENTS & FELLOWS ASSOCIATED WITH ARMED FORCES

<table>
<thead>
<tr>
<th>NAME</th>
<th>SPECIALTY</th>
<th>STATION</th>
<th>DATES IN LAB.</th>
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<tr>
<td>Bisman, Ronald</td>
<td>Orthopaedic</td>
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<tr>
<td>Fong, Juon K.</td>
<td>Neurosurgery</td>
<td>United States Public Health Services, SF</td>
<td>Jan-Mar '79</td>
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<td>Hammon, William M.</td>
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<td>Tripler Army Medical Center, Honolulu</td>
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<td>Harris, Hugh G.</td>
<td>Neurosurgery</td>
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<td>Jan '79</td>
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<td>Klemme, William</td>
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<td>Sept '79</td>
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<td>Jan '79</td>
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<td>Apr '78</td>
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