

FROM: SGHO

27 September 1973

SUBJECT: Research Proposal

TO: SGS

- I. TITLE: Tc-Phosphate complexes in the radioisotopic diagnosis of avascular necrosis.
- II. PURPOSE: We propose to investigate the use of ^{99m}Tc -phosphate complexes in the early determination of those fractures of the navicula and femoral neck which will result in avascular necrosis.
- III. BACKGROUND: Technetium phosphates are new radioactive imaging complexes recently released for general clinical and investigative use. The radionuclide ^{99m}Tc has nearly ideal physical characteristics. Its short half life, low radiation dose, ease of preparation, and high photon yield have led to extensive investigation of its use as a radiopharmaceutical. Using ^{99m}Tc as a label, several radiopharmaceuticals with an affinity for bone have been investigated. Two of the most promising agents to date are technetium-polyphosphate and technetium diphosphonate. Skeletal imaging with ^{99m}Tc -diphosphonate and polyphosphate is proving to have wide clinical applicability.

There have been no published studies which test the ability of ^{99m}Tc complexes to differentiate fractures which will heal satisfactorily from those which will not. Early identification of those fractures which will result in avascular necrosis would influence clinical decisions regarding time of weight bearing, length of casting, possible surgical intervention and prognosis of disability.

Normal bones accrete Tc-phosphate complexes to a degree sufficient to provide a discernible photographic image. If the proximal navicular fracture fragment or the femoral head is avascular, it may be possible to detect this avascular bone as a negative defect in the image. Preliminary studies show that in the immediate post-fracture period, the entire navicular area becomes scintigraphically very active. We postulate this is due to synovial hyperemia. When casted wrists are examined late in the course of fracture, the entire area of the carpal arcade is scintigraphically bright. Again, we postulate this is due to metabolic changes associated with acute reactive osteoporosis. We propose to examine patients serially, from the time of the injury, to early healing and through final healing.

IV. BIBLIOGRAPHY

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2. Subramanian, G. and McAfee, J. G.: A new complex of ^{99m}Tc for skeletal imaging. Radiol. 99:192, 1972.
3. Pendergrass, H. P., Potsaid, M. S., and Castronovo, F. P., Jr.: The clinical use of ^{99m}Tc - diphosphonate (HEDSPA). Radiol. 107:557, 1973.
4. Weiss, I. W., and Phang, J. M: Diphosphonate in a patient with myositis ossificans progressiva. Ann. Int. Med. 74:933, 1971.
5. Cram, R. L., Barmada, R., Geho, W. B., et al: Diphosphonate treatment of calcinosis universalis, NEJM 285:1012, 1971.
6. Castleman, B. (Editor), Case Records of the Massachusetts General Hospital. NEJM 288:1067, 1973.

V. TECHNICAL APPROACH: The ^{99m}Tc - phosphate complexes will be obtained from our nuclear medicine service. The research population will be comprised of both hospital inpatients and clinic outpatients. The ^{99m}Tc -complexes will be administered intravenously in doses of either 10 or 15 mg for an adult patient. Studies will be limited to those fractures of the carpal navicular and femoral neck which have a high anatomical predisposition to avascular necrosis.

The initial study will be in the first forty-eight hours following injury or at the time of diagnosis, whichever is later. Repeat studies will be performed at two and six weeks. Subsequent studies will be done as indicated by review of standard roentgenograms and/or previous studies. All radioisotope licensure requirements have been met and are on file with the medical center radioisotope committee. Radiation doses from these studies are in the range of conventional x-ray examinations. Imaging will be performed with a Ficker 5-inch Magna-scanner or a Nuclear-Chicago scintillation camera.

VI. EQUIPMENT: All equipment is on hand. Diphosphonate has been supplied at no cost from the Monsanto Chemical Corporation. Polyphosphate is supplied by Diagnostic Isotopes, Upper Saddle River, New Jersey, at a cost of \$5.00 per vial. Three patients can be scanned with the contents of one vial. Technetium will be eluted from our clinical generator at a cost of \$0.13 per millicurie.

15 mCi technetium @ 0.13/mCi = \$1.95/pt dose

3 studies per patient = \$5.85/pt

polyphosphate @ \$1.50/dose

3 studies/patient = \$4.50

total for each patient = \$10.25

The orthopaedic hand service treats approximately twenty to thirty navicular fractures per year. Injuries of the femoral head are more uncommon, numbering five to ten per year. Using these figures, maximum expenditure can be calculated thusly:

40 patients @ \$10.25 each = \$410.00

VII. INVESTIGATIVE SCHEDULE: Estimated time to completion is one year.

VIII. EXPERIMENTAL SUBJECTS: The experimental subjects will be fully informed of the nature of the study. They will be required to read and sign voluntary statements to this effect. All investigative work will be in strict compliance with AFR 169-8.

IX. USE OF DRUGS: Not applicable

X. PERSONNEL DATA:

- A. Medical Center Commander - Paul W. Myers, Brigadier General, USAF, MC
- B. Principal Investigator - Ellis P. Couch, Major, USAF, MC
- C. Associate Investigators: Eugene T. O'Brien, Colonel, USAF, MC
William C. Harvey, Lt Colonel, USAF, MC

XI. MANPOWER:

- A. Colonel, AFSC T9486, 25 hours duty time, 100 hours off-duty time
- B. Lt Colonel, AFSC 9386, 25 hours duty time, 100 hours off-duty time
- C. Major, AFSC 9481, 50 hours duty time, 200 hours off-duty time

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