5. Thermographic evaluation of calcitonin therapy in Paget's disease of the tibia

by E.F. J. RING

Royal National Hospital for Rheumatic Diseases, Bath (England)

SUMMAKY. Calcitonin has been recently introduced for the treatment of Paget's disease. Clinical assessment of therapeutic agents is difficult, as most parameters of investigation change very slowly. Thermography is able to demonstrate changes in surface temperature where an underlying pathological process is causing a vascular or metabolic disturbance. The tibia is a particularly suitable site for thermographic evaluation of Paget's disease, and the effects of treatment. A mini-computer was used to analyse the data, comparing normal and raised values from six equal areas over the tibia1 surface. The preliminary findings from four patients are shown. Each patient was receiving intermittent calcitonin therapy. Two forms of the drug are being studied, a porcine and a salmon extract. Results so far indicate that thermography used in this way is a sensitive and convenient method of assessing Paget's disease. It is a powerful research tool for the evaluation of therapeutic compounds active against the disease. An acceptable and economic treatment regime should be safely achieved by regular monitoring of those patients in need of long term therapy.

Key words: thermography; Paget's disease; calcitonin therapy; thermographic index.

Introduction

Paget's disease of the bone effects the vertebrae, pelvis, femur, tibia and skull. It is characterized by phases of destruction and repair. Destructive lesions in the long bones are usually clearly defined areas surrounded by healthy bone. The destructive phase is though to be an early manifestation of the active disease, followed by progressive bone repair. The new bone formation leads to sclerosis, expansion, and coarsening of the trebeculae. Complications of this disease include compression fractures, and osteosarcoma. Deformity is frequently seen due to bone softening especially in the weight bearing tibia and femur. The disease is poorly documented, difficulty to assess, and of unknown aetiology.

In recent years a number of agents have been used to treat Paget's disease, most have been used for inhibition of bone resorption, and have produced a temporary pain reduction. The most commonly used is Calcitonin an amino-acid extracted from pig thyroid [1'2]. The compound is administered by injection and continuous therapy is recommended. More recently a salmon extract has been successfully used. However withdrawal of treatment usually causes a relapse, hence the need for maintaining a minimum dose and deciding on the frequency of injection.

Methods of assessment are usually based on biochemical and radiological parameters. Serum alkaline phosphatase and urinary hydroxyproline excretion are most frequently reported. The latter is less convenient, requiring 24 hour urine samples and certain dietary restrictions. Radiological change is slow, it may be six months before changes are established. Isotope scans are more sensitive to the changes in the disease process.

Thermography has been used as a non invasive method of assessment of Paget's disease of the tibia. The bone lies close to the anterior surface temperature of the skin in that area. The simplicity of the examination procedure allows frequent investigations to

be made with maximum co-operation from the patient.

This paper is a preliminary report of an ongoing study to examine the use of a thermographic index as a means of assessing disease activity, and dose regime for individual patients with Paget's disease affecting the tibia.

Little is known of changes in the distribution of the disease, on and off treatment, and the presence of metabolic foci. The present study was designed to made a simple comparison of the distribution of heat over the tibia in a selected number of cases.

Technique

Rigid control of thermographic technique was maintained, which is essential for serial quantitative studies.

The patients are cooled in a room at 20°C with both legs uncovered for 15 minutes. They are then seated on a chair facing the thermograph with both feet on a low stool. As far as possible the legs are placed 10 cms apart with the tibia in a vertical position. A thermographic scan is made in 0.5 seconds with a reference temperature source set at 34.5°C. The picture is displayed in colour isotherms on a video system, and a standard region of interest selected by an on line minicomputer [4]. The area taken for measurement is a rectangle 25 cm X 5 cm wide, and is taken with the upper limit at the tuberosity of the tibia.

Reproducibility of this area is good, but changes in the degree of bowing of the tibia if present, is a limitation of the method. Other affected sites are less easily demonstrated, although the forehead and lumbar spine can produce abnormal thermographic patterns. From the area selected 500 counts are made by the computer and the temperature of each count printed out.

To facilitate analysis at a later date each printout was stored on punched paper tape. The thermographic index described by Collins and others was recorded on a temperature scale of 28.0-34.5. This index is based on calculation of isotherm areas and distri-

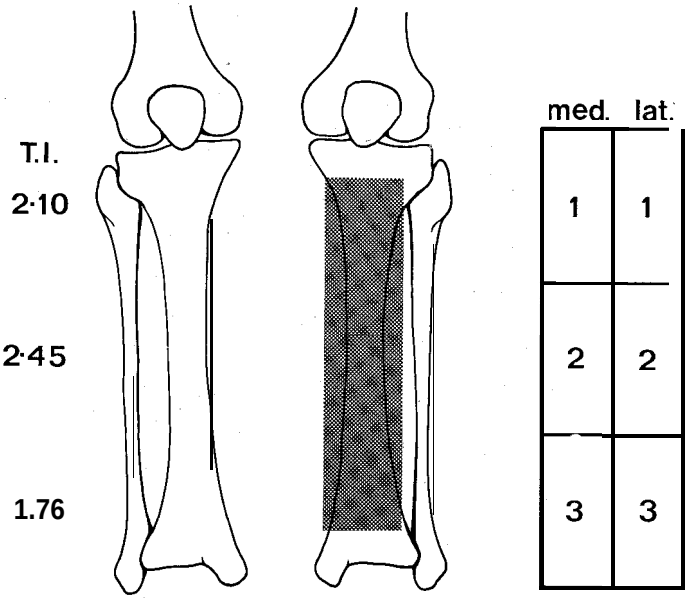
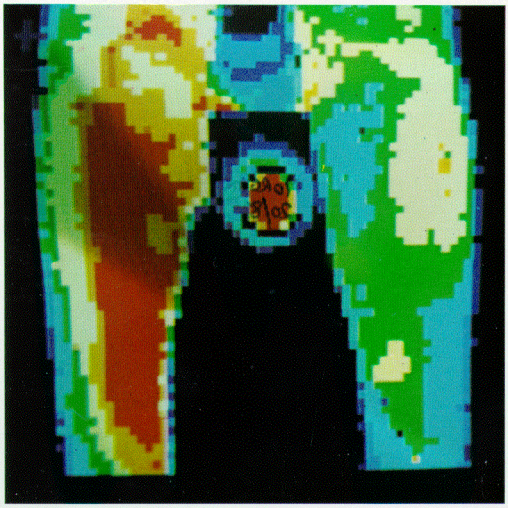
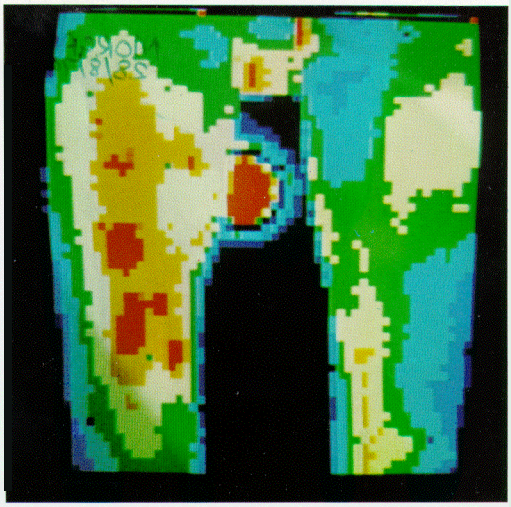


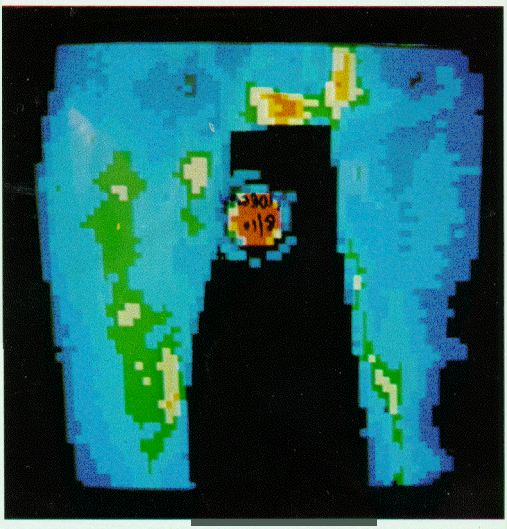
Fig. **1.** The area of thermogram quantitated showing (right) the six equal areas and (left) normal values for thermographic index at three levels, obtained from **36** thermograms in a temperature range **28-35 °C.**



A



B



C

Fig. 2 A-B-C. A) Anterior thermograms of the lower leg to show the active Paget's disease of the tibia. Red = 34.5 °C. Other colours orange yellow green blue in O.5°C below the reference (red). - B) After 1 week Calcitonin (Porcine) a reduction in temperature over the tibia is seen. C) After 6 weeks Cnlcitonin therapy the thermograms are almost normal.

bution within a defined region of a thermogram. Normal values are low 2.0 and abnormal up to 6.0.

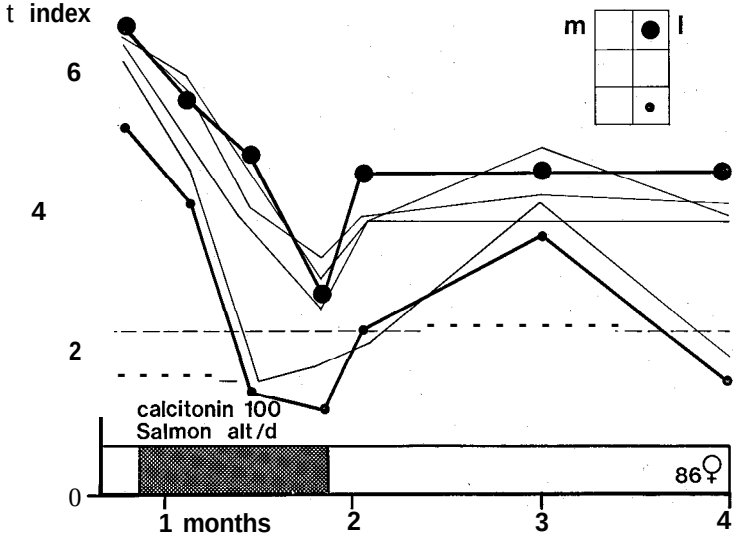
Results

Nine normal subjects aged 20-40 years were examined by thermography and scans of the anterior surface of both tibia recorded.

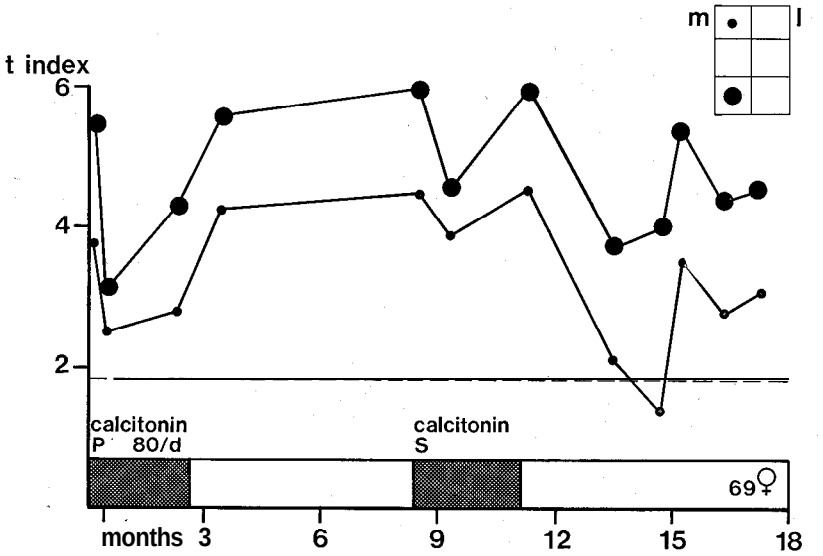
Four patients with active Paget's disease involving the tibiae were examined over a period of up to 1½ years. All four patients were given periods of treatment with either porcine, or salmon calcitonin.

The area selected for analysis in both the normal and diseased tibia was divided into six equal rectangular areas (Fig. 1). The thermographic index (TI)[4,5], was recorded in the normals and the values from both left and right legs compared using the student t. test. The results showed that there was no significant difference (p=O.6). The left and right TI values were combined to obtain the

mean for each area. The values for the six areas from each patient with Paget's disease were plotted. In each case a fall in temperature was shown very rapidly after onset of treatment by calcitonin (Graph 1, 2, 3, 4). In some cases this change could be detected in 7 days, occuring before clinical or biochemical evidence of remission (Fig. 2a,



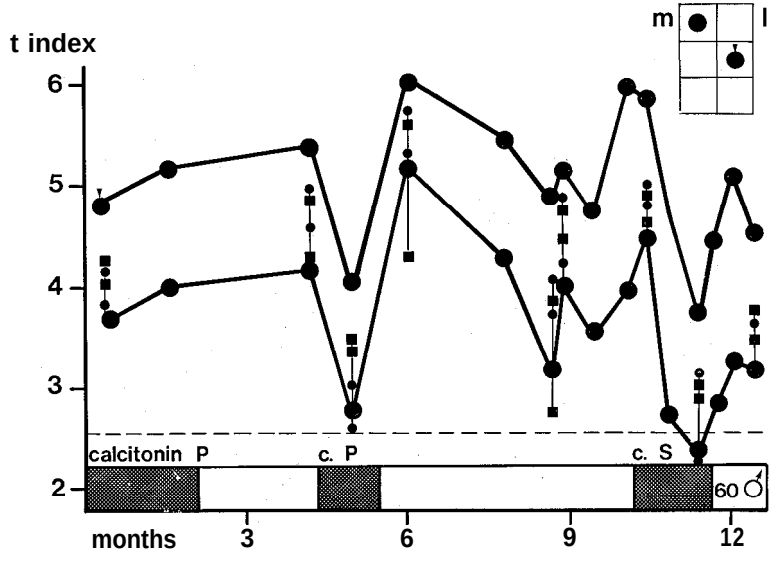
Graph. 1. Case 1. 86 years old female with Paget's disease. The thermographic index plotted from six equal areas from the tibia1 thermogram. The hottest is shown as • - • and the coldest as •-• The index falls during treatment with Salmon Calcitonin 100 MRC units given on alternate days.



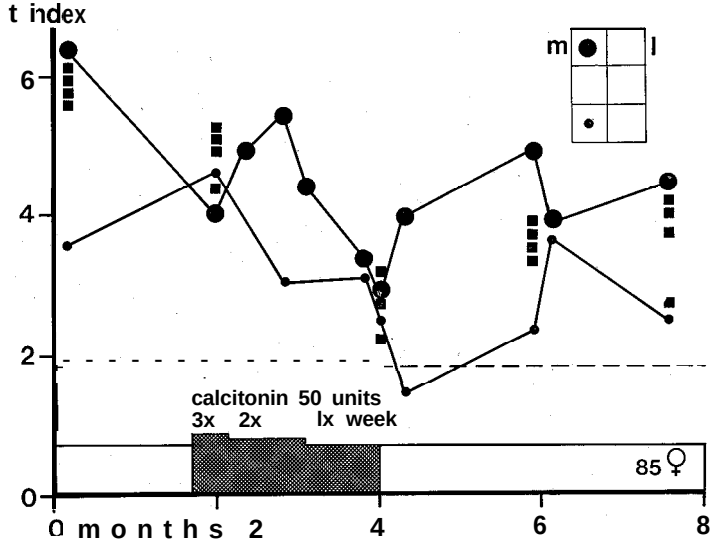
Graph. 2. Case 2. A female patient with Paget's disease. Thermographic indeces from the hottest and the coldest areas of the tibia1 thermogram recorded to show the effect of Porcine and Salmon Calcitonin therapy.

b, c). Similarly a continuous increase in the TI occured in advance of the other parameters during the period of relapse, when treatment had been discontinued. Each of the four patients with the disease exhibited a focus increased heat, in a different area of the bone.

This focus remained the hottest area both



Graph. 3. Case 3. The maximum and minimum thermographic indeces from a tibia1 thermogram of a male patient with Paget's disease treated with Porcine (P) and Salmon (S) Calcitonin. The small squares and points show the index of the other four areas of the thermogram.



Graph. 4. Case 4. Maximum and minimum thermographic indices from a patient with Paget's disease of the tibia. The effect of reducing doses of Salmon Calcitonin is seen to depress the hot focus of the diseased bone temporarily. This focus increased when therapy is stopped although the coldest continues to fall.

on and off treatment. In the cases illustrated treatment did not reduce the TI to the normal value in the focal area. Further work, which will include the comparison with clinical and biochemical studies will form the subject of a separate communication.

In a study such as this it is not only feasible to determine the effective dose of the drug but to determine the anticipated frequency of maintenance dosage (Graph 4). Calcitonin is very expensive, and the recommended daily injection, limits its use both for financial and convenience reasons. Resistance to porcine calcitonin therapy has been reported, after long term administration. It is not yet known if this is an immune antibody reaction or compensating parathyroid hormone secretion. Salmon calcitonin is more potent and needs more clinical evaluation. It is clear that thermography can be used to demonstrate metabolic changes within the tibia, and enable the more economic and efficient use of long term therapy[6].

REFERENCES

1. BELL N.H., AVERY S., **JOHNSTON C.: Effects** of calcitonin in Paget's disease and polyostotic fibrous dysplasia. *J. Clin. Endocrin.,* 31, *283-290, 1970.*
2. **HADDAD** J. G., **BIRGE S. J., AVIOLI L. V.: Effects** of prolonged thyrocalcitonin administration on Paget's disease of bone. New *Engl. Jour. Med., 283, 549-555, 1970.*
3. **RING E. F. J., COLLINS A. J., BACON P. A.:** Computerised thermography of peripheral joints (in press).
4. **COLLINS A. J., RING E. F. J., COSH J. A., BACON** P. A.: Quantitation of thermography in arthritis using multi isothermal analysis. I. The Thermographic Index. *Ann. Rkeum. Dis., 33,* 113-115, 1974.
5. RING E. F. J.: Thermography and rheumatic diseases, in: *Thermography,* Bibliotheca Radiologica, No. 6. Karger (Basel) 97-106, 1975.
6. **COLLINS A. J., RING E. F. J., BACON P. A., BROOKSHAW** J.: Thermography and radiology. Complimentary methods for the study of inflammatory diseases. *Clinical Radiology, 27, 237-243, 1976.*

Acknowledgments

The assistance of, Dr. J. R. Barker of the University of Bath with data processing and Dr. J. Davies of the Royal National Hospital is gratefully acknowledged.