THE INVESTIGATION OF RADIUM DEPOSITION IN THE HUMAN SKELETON BY GROSS AND DETAILED AUTORADIOGRAPHY

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INTRODUCTION

Some of the radioelements, when taken into the body, are deposited principally in bone after a relatively short period of time. After being deposited they become firmly incorporated so that elimination is extremely slow. It is well established that most bone-seeking radioelements are deposited in an irregular manner and that they have a destructive effect on bone. The meager information available on the manner of deposition and effects of heavy bone-seeking radioelements is that obtained from luminous dial workers. In most instances varying amounts of three bone-seeking radioelements were used in the luminous material; namely radium, mesothorium, and radiothorium.

In 1926 Martland(1) reported the irregular deposition of radioelements in the maxilla and femur of a patient aged twenty-four who died after seven years employment. Hoecker's(2) reported autoradiographic findings in two luminous dial workers, one patient aged thirty-two and another aged thirty, who died seven and ten years, respectively, after leaving the industry.

The principal source of clinical material for the present investigation of the manner of deposition of radium are patients who were given

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radium salts therapeutically and persons who were employed as luminous dial painters from about 1915 to 1930. A clinical investigation of a large number of these patients has been carried on in this laboratory for the past two years.

We have been fortunate in obtaining specimens from two patients who received only radium salts and from one luminous dial* worker. This is the first time that large amounts of fresh human bone have been carefully studied to determine the precise pattern of distribution of the heavy radioelements. In these cases, the radioelements have been present in the body for a much longer time (17, 22, and 24 years) than the studies on the luminous dial workers (7 and 10 years) and it is also the first opportunity for an extensive study of one heavy radioelement (radium).

The following are brief summaries of the case histories of these patients and of the specimens obtained:

1. A 48-year-old female who died in 1951 from fibrosarcoma of the foot. She received radium water twenty-two years previous to her death for a condition diagnosed as "migratory polyarthritis". The femur, humerus, tibia, fibula, and skull were obtained for study.

2. A 51-year-old female who had a reconstruction operation on the head of the femur for asceptic necrosis in 1951. She had received radium chloride intravenously 17 years previously for mental depression. Specimens from the greater trochanter, head of the femur, and fibula were obtained.

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* We have not established the presence of mesothorium or radiothorium in the specimens from the patient.

3. A 48-year-old female who worked as a "luminous dial" painter from 1921 to 1927 and who died in 1951. Fourteen years prior to her death the patient had multiple fractures of the femora, osteomyelitis of the mandible, and other complications attributed to radium poisoning. Specimens from the vertebrae, ilium, and ribs were obtained.

<u>TECHNIQUE</u>: GROSS AUTORADIOGRAPHS

We have used a technique similar to that described by Lotz[3]. The bones were serially sectioned with a band saw, the slices varying from 2 to 8 mm in thickness depending upon their ultimate use. All bones were kept in the deep freeze from the time of the autopsy or operation until sectioning to preserve the histological structure as much as possible. Just prior to cutting, the bones were placed in dry ice. The sections were cleaned with acetone after cutting to remove any bone dust which might be present. Since they were frozen it did not appear that cutting caused any distortion of the distribution pattern in the autoradiographs. The bone sections were placed between no-screen X-ray* film so that autoradiographs of both sides of the sections were obtained. The films were placed on a board having the same dimensions as the X-ray film to provide a rigid flat surface. The first layer was covered with corrugated board and a second layer of film and bone sections was placed on this. The bone sections were flat enough so that contact with the film was good. If a section contained much marrow, it was coated with a 1% solution of celloidin to minimize chemical fogging of the film. Each layer was held together with

* Kodak

rubber bands, care being taken to avoid effects of pressure on the film. Several layers were placed in a large porcelain tray, packed with creped wadding to prevent shifting, and sealed to light by taping corrugated board over the top of the tray. The procedure was performed as quickly as possible to avoid thawing of the bone, and the specimens were then returned to the deep freeze.

RESULTS: GROSS AUTORADIOGRAPHY

Skull: There were small circular areas of radium concentration randomly distributed throughout the coronal sections of the skull. These were rather sharply defined and ranged from areas so small that they could just be visualized to 2 mm in diameter. In some sections, these areas were uniformly distributed throughout. In other parts, they were more numerous toward the outer table and in others toward the inner table. In some sections, these areas of concentration were more numerous in the sagittal and coronal suture lines, still in others they were concentrated along the superior or inferior surface so that they appeared to outline the interior or superior margin of the skull. There were also diffuse areas usually measuring 2 to 5 mm in diameter. These areas are probably the result of the combined effects of a number of smaller areas. In general, radium seemed to be more concentrated in the diploe than in the more dense surrounding bone (Figure 1).

Humerus: In the trabecular bone of the head of the humerus there appeared areas of concentration about 1 to 3 mm in length and 1 to 2 mm in width which were adjacent to the articular surface, principally near the medial inferior border*. A 1- to 2-mm area of lesser density usually was present

* The humeral and femoral heads have been arbitrarily divided into four quadrants to more accurately localize the areas of concentration.

between the areas of concentration. There were smaller areas randomly distributed throughout the head similar to those seen in the skull. Longitudinal areas of radium concentrated in the cortex usually measured from .3 to 1 mm in width and from 1 to 3 mm in length. These areas were randomly distributed throughout the cortex and were more frequent in the proximal one-half of the shaft. In addition, there was diffuse darkening of the film in certain areas of the cortex.

Femur: The entire head of the femur was outlined by a linear concentration of radium 1 mm in thickness. Just beneath the articular cartilage the greatest concentration was around the inferior medial quadrant.

There were small rather sharply defined areas of radium concentration scattered throughout the bone architecture of the head varying from pinpoint size up to 1 mm in diameter. These small areas extended down into the neck and shaft as trabecular bone was present. In some sections these concentrations were closely grouped in areas .5 to 1 cm in size surrounded by similar areas with a diffuse, less dense darkening of the film. In general, there was more radium concentrated in the lower part of the head and more in the medial than lateral quadrant.

There was an area of concentration 1 x 4 cm in size in the medial cortex at the level of the lesser trochanter. There was another area, 1 to 2 cm in length and 3 mm in width, which outlined the superior surface of the greater trochanter.

In the midsection of the medial aspect of the shaft there was a linear area of concentration about 1 mm in width and 10 cm in length near the periosteum. As in the shaft of the humerus there were longitudinal areas of concentration which were randomly distributed throughout the cortex (Figure 2). They were .3 to 2 mm in width and usually 3 to 5 mm in length. In some instances, however, they extended as far as 10 to 15 mm. In general, these areas were more frequent near the periosteum. In some areas there was deposition near the endosteum and periosteum outlining the cortex. The areas were more frequent in the proximal end of the shaft as in the humerus and more frequent in the cortex of the medial one-half of the shaft than the lateral one-half. There was a linear area of concentration surrounding the distal end of the femur both sub-articularly and on its lateral aspects, 1 mm in width. In this diffuse linear concentration were small more dense areas about .5 mm in diameter.

Tibia: The linear area of concentration of radium around the proximal end and sub-articularly was present in the tibia as in the other long bones. Similar small irregular distributed areas of concentration were also present in the trabecular bone of the tibia as in other trabecular bone. In several sections, these areas were more frequent in the metaphyses and in a few sections there was a vague horizontal outline of the sclerotic zone of diaphyseal and epiphyseal union. This horizontal outline of the sclerotic zone was more distant and narrow in the distal end of the tibia.

There were similar longitudinal areas of concentration occurring in the cortex of the shaft of the tibia as in the femur and humerus. In general, they were considerably less frequent than in the other bones. As in the femur, they were more frequent on the medial side of the shaft. The most significant difference between the tibia and other long bones was that almost all of these concentrated areas were near the periosteum (Figure 3).

Fibula: In the fibula, almost all of the activity appeared in the trabecular bone at the proximal and distal ends. Very few small longitudinal areas of concentration were noted in the cortex of the shaft of the fibula similar to those observed in the other long bones. The five weeks exposure for the shaft of the fibula was not long enough to give a satisfactory distribution pattern.

ROENTGENOGRAPHIC CHANGES

We have observed roentgenographically areas of decreased density in the cortex of the shafts of the long bones, and these were of similar dimensions to the areas of radium concentration found in the gross autoradiographs. These areas of decreased density were found to be macroscopic areas of necrosis. In preliminary work to ascertain the relationship, if any, between these macroscopic necrotic areas and radium deposition, no concentrations of radium have been found in or around these areas[4].

TECHNIQUE: DETAILED AUTORADIOGRAPHS

We have continued the work initiated by Dr. James Arnold[5,6] in this laboratory. In earlier studies of detailed autoradiographs it frequently happened that the specimen selected contained little or no activity, and extremely long exposures were necessary. This possibility has now been minimized by using the gross autoradiographs as a guide for selecting specimens from concentrated areas. The gross autoradiographs and roentgenographs were placed on an X-ray view box. When viewed simultaneously, concentrated areas showing roentgenographic changes, or both could be outlined on a thin sheet of paper placed over the gross autoradiograph or roentgenograph. This paper, on which the outline of the bone slice had previously been recorded, was an accurate guide for taking specimens for detailed autoradiographs. It also served as a permanent record of the exact location from which the specimen was taken.

These samples of bone, .5 to 1 cm in width and 1 to 2 cm in length, were fixed in acetone and imbedded in a mixture of celloidin and diamylphthalate. This method was devised particularly for obtaining thin sections of bone containing radioelements; it has two particular advantages. Routine procedures of fixation have been found to leech radioelements out of bone. Similarly any attempt to de-calcify the bone may distort the distribution pattern. This method enables one to cut serial sections, 6 to 12 microns in thickness, from blocks of un-decalcified bone. However, it is not as satisfactory for obtaining thin cross sections of dense cortical bone. Cross sections, 50 to 150 microns thick, were obtained from this dense cortical bone by a different technique which was satisfactory for autoradiographs. The piece of bone is mounted on a platform and held in place firmly by sharp prongs. The platform can then be moved in three planes so that the bone may be oriented for cutting with a small stationary rotary saw(7).

A photographic emulsion about 5 to 10 μ thick is placed over these histological preparations following established techniques(8). The slides are placed in boxes and sealed from light and humidity. After suitable exposure, which can be determined by varying the length of time the slides are exposed, the autoradiograph is developed. The sections are then stained using hematoxylin as a regressive stain, i.e., the sections were overstained and then the stain removed from the photographic emulsion as much as possible. Histological details and radioelement distribution can now be observed simultaneously.

RESULTS: DETAILED AUTORADIOGRAPH

In general, radium was found to be concentrated in about 5 to 15 of every 50 Haversian systems observed in cortical bone. In the sections from which the photomicrographs of Figures 4, 5, and 6 were taken, almost no activity was observed except in this small percentage of Haversian systems and in interstitial lamellae in which radium was rather heavily concentrated. Within the Haversian systems the radium might be confined primarily to one or two concentric lamellae, as shown in Figure 4, or the greatest concentration might be found around the periphery of the central canals of periphery of the Haversian system itself. In others it was found distributed throughout the system. Note in Figure 4 the lighter concentration of radium in the interstitial lamellae between the two Haversian systems with heavy radium concentration and the Haversian systems above and below free of alpha tracks.

In Figure 5 the microscope was focussed on the underlying histological structure. Observe that the Haversian system in the upper left has undergone extensive destruction and the other Haversian system in the lower left, which has radium concentrated, is relatively normal except for an apparent occlusion of the central canal. The Haversian system in the lower central part of the photomicrograph did not have any radium present. It will be noted, however, that the central canal is increased in size and filled with an amorphous material. One of the most interesting things which occurred is the darkening over the two concentric lamellae in which the alpha tracks were more concentrated. This more clearly delineates the area of deposition of radium within the ~~H~~aversian system than in Figure 4. This darkening was not observed until seen on the photomicrograph. Figure 6 shows a distinct linear concentration of radium deposited in an interstitial lamella gradually falling off to the left. The proximal end of an area of destruction, 100 microns in length, is present in the upper right corner of the photomicrograph. No alpha tracks were present.

In trabecular bone, the areas of concentration of radium were usually about 5 to 15 microns in the greatest diameter and, as in Figures 7 and 8, assume almost any configuration. The trabecula on the left has one small area of concentration on the superior surface. In sections exposed for much shorter lengths of time the diffuse scattering of the alpha tracks seen throughout the section were not usually observed. In Figure 7 there is a linear concentration of radium on the superior side of the area of greatest concentration which runs parallel to the curvature of the trabecula for a distance of 40-50 microns. These linear areas of radium concentration were also noted in cementing lines of contact bone.

In some areas, several adjacent trabeculae had these areas of concentration while in others a large number of fields could be observed which were relatively free of radium.

DISCUSSION

The availability of large amounts of fresh human bone has permitted us to obtain a comprehensive picture of radium deposition throughout the skeleton by serial gross autoradiographs and to study the precise manner of deposition of radium in compact and trabecular bone by serial detailed autoradiographs.

In the trabecular bone the areas of concentration are usually pinpoint to .5 mm in diameter. A large number of the areas may be seen rather closely together giving an impression of much larger concentration. These small areas of concentration were so numerous at the junction of the articular cartilage and bone that they appeared grossly as an outline of the contour of the articular surface. This outline was usually about 1 mm in thickness and in some instances extended round on the lateral aspects so that the entire proximal or distal end of the bone would be outlined. In some bones, a vague horizontal line of concentration was formed by an increase in frequency of these small areas at the junction of the diaphyses and epiphysis.

Martland's gross autoradiographs of the luminous dial worker were so indistinct that we were unable to make comparison between his findings and the results of this investigation.

Confirmation that the darkened areas on the X-ray film resulted from the alpha emission of radium was made by detailed autoradiography. The same random distribution observed grossly was found microscopically. These small areas were usually about 5 to 15 microns in diameter and were seen at varying depths within the trabeculae. However, there were wide variations in size and shape of the areas of concentration. In certain areas a considerable number of trabeculae was found to have heavy concentration of radium. This was rather striking at the junction of the trabecular bone and cartilaginous disc of the vertebrae of the luminous dial worker. In some sections of this patient almost all of the trabeculae adjacent to the cartilage had heavy concentrations of radioelements. No significant difference has been observed in the microscopic examination of the detailed autoradiographs of trabecular bone of this patient and the patients who were known to have received only radium.

Similar correlation was made between the gross and detailed autoradiographs, usually measuring .3 to 1 mm in width and up to 15 mm in length grossly, were found to result from the concentration of radium in the surprisingly small percentage of Haversian systems and in interstitial lamellae of the same bone.

The finding of the random distributions of concentrations of radium such as the linear and small irregular areas of concentration in trabecular bone and the concentrations in cementing lines and in the small percentage of Haversian systems in compact bone supports the general impression that radium is deposited in areas which are metabolically active at the time of administration or re-distribution. The diffuse and more uniform distribution seen in sections exposed for longer periods of time may be the result of a different mode of deposition such as ion exchange(9).

We have not attempted any quantitation at this time. Grossly, it does appear that the bones having the most radium, determined by physical means, have an increase in frequency of Haversian systems containing radium. We have not found the uniformity of distribution within the Haversian system reported by Hoecker. In most instances the greatest concentration is confined to one or two concentric lamellae with considerably less concentration in the remainder of the Haversian system. This could be the result of (1) the longer period of deposition - 7 to 10 years as compared to 17, 22, and 24 years, (2) the difference in deposition of mesothorium and radiothorium and radium in the luminous dial workers as compared to radium in most of our material, (3) or differences in techniques or selection of specimens. The most likely possibility is that the specimens selected had Haversian systems which only had a uniform distribution.

The chief advantage of the method we have used is that the manner of radium deposition and bone destruction may be determined grossly and that this information can be used for accurate selection of specimens for study of bone histopathology and detailed autoradiographs. Specimens can be accurately selected from areas showing destructive changes roentgenographically and/or from areas of concentration of radium seen grossly. By placing the bone specimen on thin paper on an X-ray view box the outline of the specimen may be quickly made. This outline is then placed over the autoradiograph or roentgenograph and the exact area for detailed autoradiographs and histological specimens sketched on the outline of the bone. This outline is then placed adjacent to the bone so that the exact level and area may be marked on the bone. The paper is a very convenient and accurate record of the specimens, so that the gross autoradiographs and roentgenographic changes may easily be referred to in the study of histopathology as well as detailed autoradiographs. We have not used the gross autoradiographs to determine the exact dimensions of the areas of concentration in bone because of the lack of resolution. Its principal advantages are: (1) a comprehensive picture of the manner of distribution throughout the skeleton is given, (2) the approximate dimensions of the areas of concentration may be obtained and (3) it serves as a useful guide for the selection of concentrated areas in which the exact dimensions may be determined from detailed autoradiographs. This procedure has a wide range of potential usefulness in clinical investigation using radioisotopes and in the more accurate evaluation of therapeutic effectiveness of the gross autoradiographs.

As in most procedures, complete reliance cannot be placed on the results of the gross autoradiographs. On a few films, obvious chemical fogging was present as a result of liquid from the marrow. It is known that pressure will cause darkening of film. However, care was taken to minimize these factors. In general, we consider this method accurate and reliable because of definite confirmation of the gross findings by detailed autoradiographs and the satisfactory results obtained by other investigators.

If radon gas, the first daughter element of radium, is diffusing around in the specimens of bone before application of the photographic emulsion or through the emulsion during exposure, to a significant degree, it may introduce difficulties, especially in any attempt to estimate any amount of radium necessary to produce bone damage. We consider that the gas would not be of significance in this investigation since there should be a uniform loss throughout and we have been primarily interested in the qualitative aspects of deposition thus far.

In general, our observations are similar to those of other investigators. Radium is deposited in an irregular manner in different bones as well as within the same bone. We are avoiding the obvious conclusion that a direct relation between macroscopic areas of destruction and radium concentration exists because both are of the same dimensions, as well as explaining the failure to find radium concentrated in or around these necrotic areas by saying that by the time they become necrotic the radium has been removed. This may, and in some instances probably does, occur.

The avoidance of this conclusion is based on failure, thus far, to find areas of transition in which both roentgenographic change and radium concentration were present and the presence of destructive changes within the i.e. Haversian systems in the presence or absence of concentrations of radium. It should be apparent that the difficulties involved in reconstructing a pathological process of 20 to 30 years duration from specimens obtained at the termination or at one stage of the process are many.

SUMMARY AND CONCLUSIONS

A comprehensive and precise pattern of the mode of deposition of one heavy bone-seeking radioelement (radium) in human skeleton has been obtained.

In general, it was found in small areas of heavy concentration irregularly distributed in both cortical and trabecular bone.

In trabecular bone these areas of concentration were usually 5 to 15 microns in the greatest dimension and were found at any depth within the trabecula. There was a wide variation in size and shape of these areas and in some instances linear concentrations ran parallel to the curvature of the trabecula, 50 - 100 microns. At the junction with the articular cartilage of such bones as the humerus, femur and vertebra heavy and rather uniform concentrations in the trabeculae were present and appeared as a 1-mm linear outline of the entire articular surface of the bone on gross autoradiographs. In some bones, the metaphyseal-epiphyseal junction was indistinctly outlined by an increase in frequency of these small areas of concentration. The skull had more small areas of concentration than the other bones and these were more frequent in the diploe than in the dense tables.

As in trabecular bone in which only a small percentage of the trabeculae had small concentrated areas of radium, compact bone had only a small percentage of the Haversian systems and interstitial lamellae in which radium was concentrated. There was a random distribution of the Haversian systems and interstitial having radium concentrated. However, they were usually more frequent nearer the periosteum. The length of these areas of concentration was usually 1 - 5 mm. However, in some instances there were 10 - 15 mm within the Haversian system in a large number of instances radium was most concentrated in only one or two concentric lamellae. Some cementing lines were clearly outlined by heavy concentrations of radium. In some sections exposed for long periods of time there was a much less concentrated and more uniform distribution of radium. These findings are in agreement with existing theories that radium has more than one principal mode of deposition. The small, highly concentrated areas may have been areas in which bone formation was taking place at the time of administration or redistribution of the radium. The more uniform and less dense distribution may have resulted from inorganic ion exchange.

The macroscopic areas of destruction found in the roentgenographs and the areas of radium concentration on the gross autoradiographs have served as a guide for the accurate selection of specimens for study of the deposition of radium microscopically and of the histopathological changes.

We have substantiated the well established fact that heavy bone-seeking radioelements cause bone destruction. We have avoided, at present, the obvious conclusion that a direct relation between necrotic areas and areas of radium concentration exist because of many difficulties involved in the reconstruction of a pathological process of such long duration. Additional information from the work in progress may give a better understanding of the relationship between the deposition of radium and the histopathological changes.

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Figure 1. These are three gross autoradiographs of coronal sections of the skull of patient No. 1 exposed for 5 weeks. Note the variation of the size of the areas of concentration and how, in certain areas, they are grouped so closely together that they appear as one large concentration. The light area just to the left of the center of the second section is probably due to poor contact on the film. In the center of the third section very small areas of concentration outline the inner table.

Figure 2. These are autoradiographs of two longitudinal sections of the cortex of the femur. The smaller section was taken 2 mm from the periosteum and the larger section cut just medial to it. The areas of concentration are more frequent in the smaller section and the upper end of the larger section which were nearer the periosteum. The large area of darkening in the center of the larger section is probably the result of an endosteal concentration of radium, since this surface was on the periphery of the marrow cavity.

Figure 3. This is an autoradiograph of an entire section of tibia demonstrating the irregularity of distribution of radium in trabecular bone. The small areas of concentration seen in the proximal end extend down into the shaft as far as the trabecular bone extends. In the distal end the concentration is near the articular surface. The vague outline of the "sclerotic zone" of the metaphyseal-epiphyseal junction cannot be seen in this section. It does show the linear area of concentration adjacent to the articular cartilage. In the cortex of the shaft the areas of concentration are not frequent, however, they are more numerous in the medial shaft and near the periosteum of both shafts. Observe the diffuse less dense outline of the shafts.

Figure 4. This is a detailed autoradiograph of a cross section of cortical bone from the humeral shaft of patient No. 1 exposed for 50 days. These are two of the small number of Haversian systems having radium concentrated in this section. The most concentration is in two concentric lamellae in the center of the Haversian system. The alpha tracks are less dense in the remainder of the Haversian systems and the interstitial lamellae between the systems. Observe that the activity suddenly falls off around these areas of concentration and the rest of the photomicrographs are relatively free of alpha tracks.

Figure 5. This is a photomicrograph of the bone underlying the detailed autoradiograph of Figure 4. Note the dark concentric rings outlining the lamellae having the greatest concentration of radium. The central part of the Haversian system in the upper left is undergoing destructive changes. Figures 4 and 5 demonstrate how radium concentration and histopathological changes can be studied at the same time.

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Figure 8. (134-day exposure). Patient No. 2. The trabecula in the upper right has radium concentrated in the center. The one on the left has one small concentrated area at its superior border with random distribution throughout.

BIBLIOGRAPHY

(1) Martland, H. S. 1926. Microscopic changes of certain anemias due to radioactivity. Arch. Path. and Lab. Med. 2: 465

(2) Hoecker, F. E., Roofe, P. G. 1951. Studies of radium in human bone. Radiology Vol. 56, No. 1. pg. 89-98, January.

(3) Lotz, W. E., Gallimore, J. C., Boyd, G. A. 1952. How to get good gross autoradiographs of large undecalcified bones. Nucleonics. Vol. 10, No. 3. pg. 28-31, March.

(4) A progress report of clinical studies on twenty-four patients compiled by William B. Looney. ANL-4666. 1951.

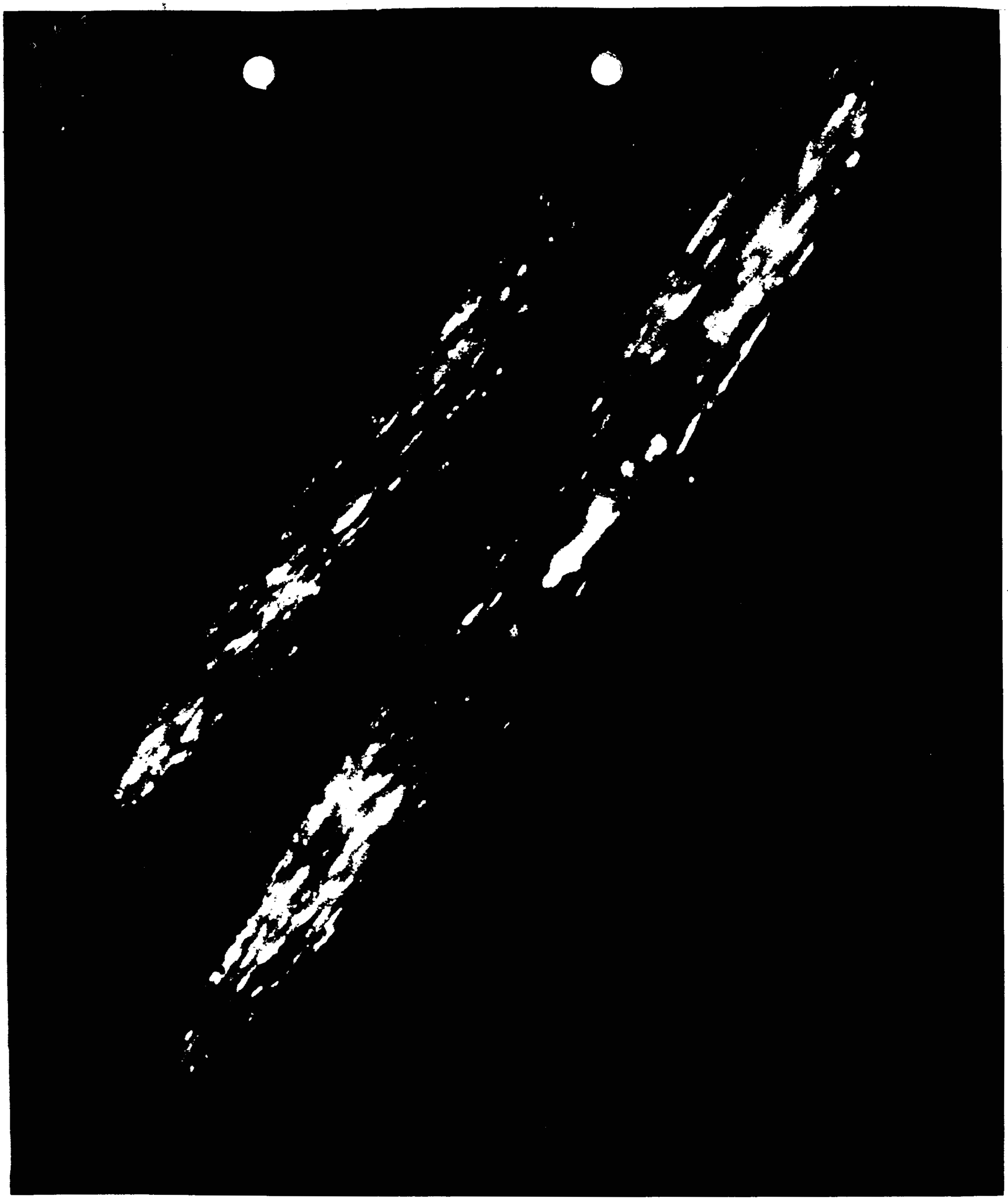
(5) Arnold, J. S. 1951. A method for embedding undecalcified bone for histologic sectioning, and its application to radioautography. Science Vol. 114, No. 2955. pg. 178-180, August 17.

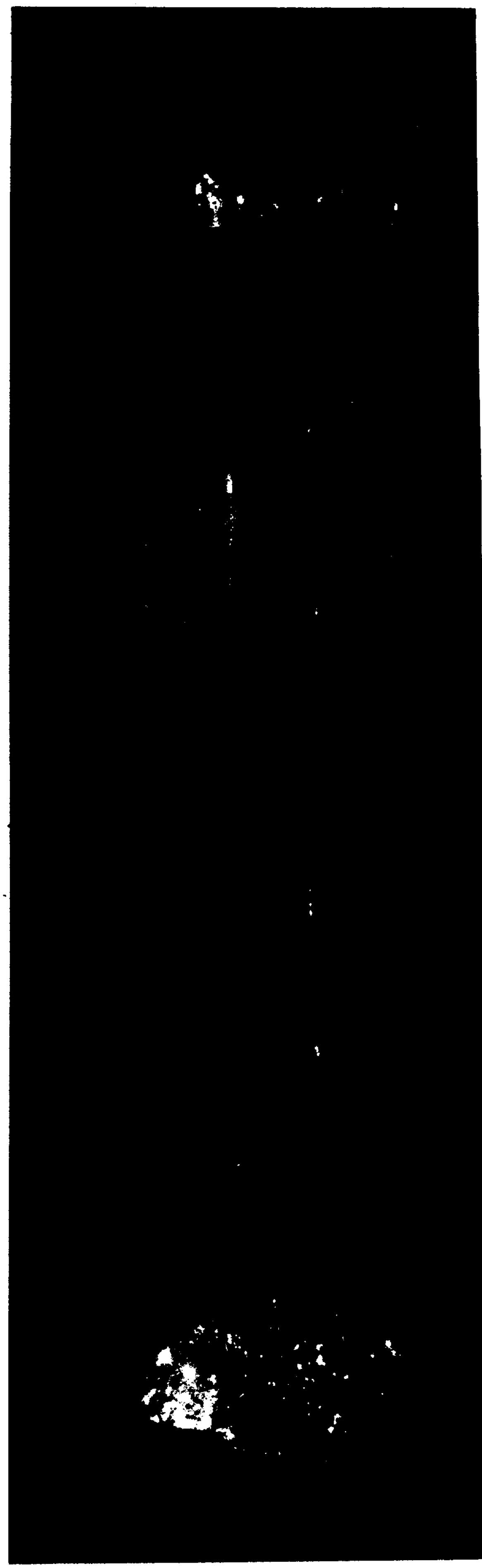
(6) Arnold, J. S. 1951. Progress report radioautography. ANL-4625.

(7) Roofe, P. G., Hoecker, F. E., Voorhees, C. D. A rapid bone sectioning technic. Proc. Soc. Exper. Biol. and Med. Vol. 72, pg. 619-622. 1949.

(8) Gross, J., Bogoroch, R., Nadler, N. J., Lablond, C. P. 1951. The theory and methods of the radioautographic localization of radio-elements in tissues. Amer. Jour. of Roent. and Rad. Therapy. Vol. 55, No. 3. pg. March.

(9) Schubert, J. 1951. Estimation of radioelements in exposed individuals. Nucleonics. Vol. 8, No. 2. pg. 13-28, February.





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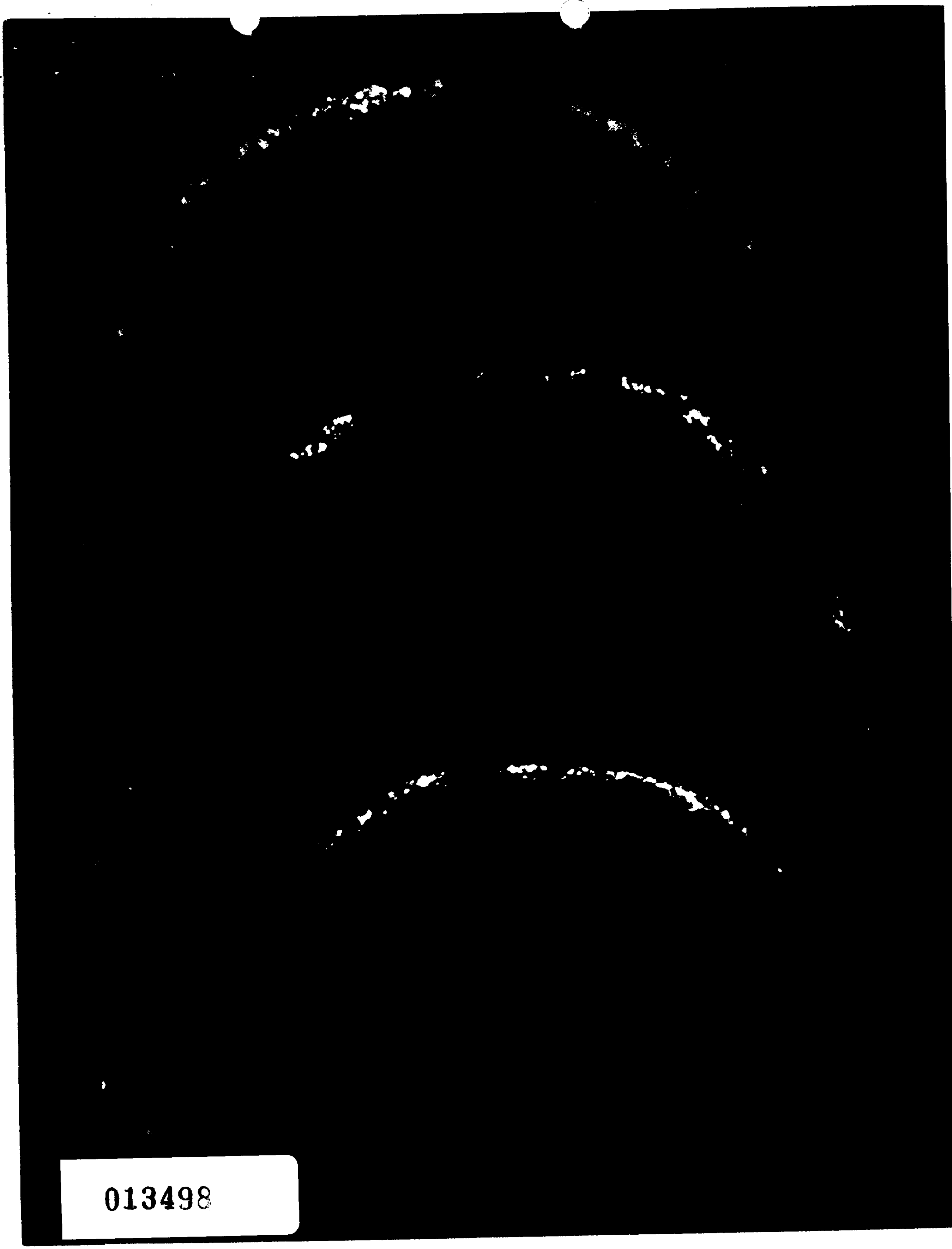
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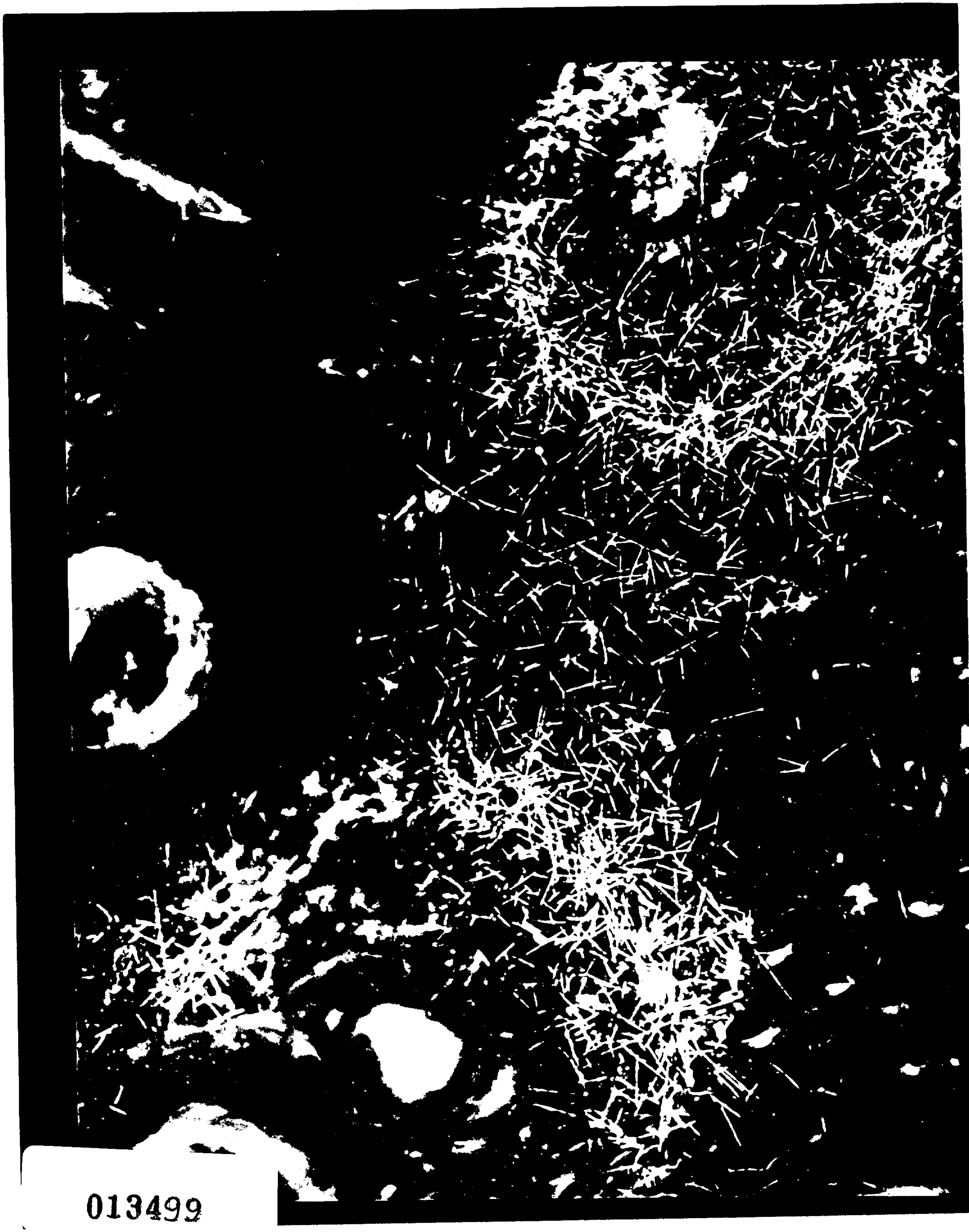

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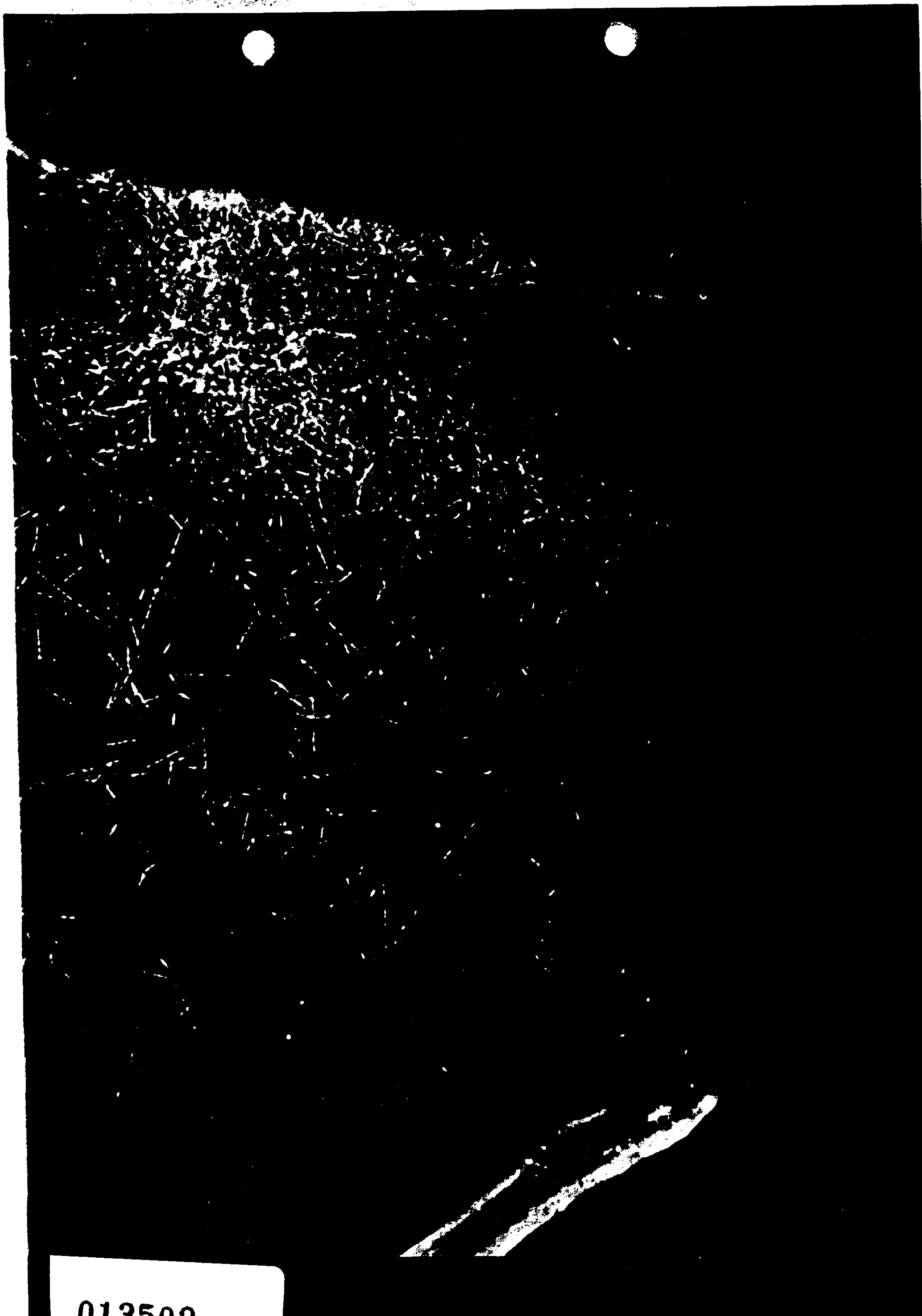
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