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(54) **Titre : DETECTION DE CARENCES NUTRITIONNELLES INFLUENCANT LA SANTE OCULAIRE**
(54) **Title: DETECTION OF NUTRIENT DEFICIENCIES INFLUENCING OCULAR HEALTH**

(57) **Abrégé/Abstract:**

The present invention provides methods for identifying and treating subjects having nutrient deficiencies. A method for scoring nutritional deficiency in a subject's eye is also provided.



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1 **DETECTION OF NUTRIENT DEFICIENCIES INFLUENCING OCULAR HEALTH**

2 CROSS REFERENCE TO PRIOR APPLICATIONS

3 **[0001]** This application claims priority under the Paris Convention to US Provisional
4 Patent Application 61/884,623 filed September 30, 2013 which is incorporated herein by
5 reference.

6 FIELD OF THE INVENTION

7 **[0002]** The field of invention relates to methods and compositions useful for detecting,
8 diagnosing, preventing and treating ocular diseases and corresponding nutrient deficiencies
9 and microvascular non-perfusion.

10 BACKGROUND OF THE INVENTION

11 **[0003]** Ocular health and disease is a global concern, particularly given the ageing
12 population in many countries. Ocular health is thought to decrease naturally with age, and
13 can be compromised by oxidative stress, illness and visual stresses, such as prolonged
14 exposure to visual display monitors (U.S. Patent Application Publication No 2012/0258168).

15 **[0004]** Nutrition is one feature of ocular health that has been studied in age-related
16 ocular diseases, such as age-related macular degeneration (AMD). Macular degeneration is
17 a chronic eye disease that causes vision loss in the central field of vision. Dry macular
18 degeneration is marked by deterioration of the deep layers of the retina. Wet macular
19 degeneration is characterized by blood vessels that grow under the retina, leaking blood and
20 fluid. The pathology of AMD is believed to be caused, at least in part, by oxidative damage
21 (Beatty et al., Surv. Ophthalmol. 2000, 45:115-134; Cai et al., Prog. Retin. Eye Res. 2000,
22 29:263-271). The healthy eye contains antioxidant molecules, including enzymes, vitamins
23 C and E, omega-3 fatty acid docosahexanic acid (DHA) and macular pigments lutein and
24 zeaxanthin. Deficiency of antioxidants in the ageing eye is believed to be a risk factor for
25 development of AMD (Ocular Nutrition: It's Role in Maintaining Eye Health, Module 1:
26 Nutrition and Health of the Aging Eye, 2011, 6 pages). It follows that nutrient supplements,
27 including antioxidants such as, zinc, vitamin C, vitamin E, beta carotene, lutein, zeaxanthin
28 and omega-3 fatty acids, are sometimes recommended to prevent AMD progression and
29 improve vision.

1 [0005] Lutein and zeaxanthin are xanthophyll carotenoid pigments found in the retina.
2 Subjects having AMD are known to have decreased amounts of lutein and zeaxanthin in
3 their retina. Some studies suggest that visual acuity, contrast sensitivity, and the amount of
4 retinal pigment in the human eye can be improved as a result of lutein and zeaxanthin
5 supplementation or a combination of these xanthophylls with other antioxidants (Stiles et al.
6 (2004) Optometry, 75:216-230). Other studies suggest that macular pigment optical density
7 (MPOD), a measure of the amounts of lutein and zeaxanthin in the macula of the living
8 human eye, is a marker of the health of the human eye (U.S. Patent Application Publication
9 No. 2012/0070422).

10 [0006] Nutritional supplements including lutein and zeaxanthin have also been
11 suggested to promote ocular health and treat "ocular diseases" (see, for example, U.S.
12 Patent Application Publication Nos. 2010/0068298 and 2012/0258168). However, the range
13 of "ocular diseases" appears to be limited to early stages of AMD and related ocular
14 disorders thought to be associated with oxidative stress (U.S. Patent Application Publication
15 No. 2010/0068298). The favored dosage of lutein and zeaxanthin has been 10 and 2 mg,
16 respectively, often provided to subjects in combination with omega-3 fatty acids and one or
17 more antioxidant nutrients, such as Vitamin C, Vitamin E and zinc, which were included in
18 the AREDS 2, wherein the composition was tested on patients having moderate to severe
19 AMD (e.g., The AREDS2 Research Group, JAMA 309:2005-2015, 2013). However, these
20 nutrients are not known to reduce the risk of progression to advanced AMD or to treat
21 moderate to severe AMD.

22 [0007] Methods for identifying nutritional deficiencies by way of an eye exam are
23 desirable. Nutritional treatment of nutritional deficiencies identified by way of an eye exam is
24 desirable.

25 SUMMARY OF THE INVENTION

26 [0008] In a first aspect, the present invention provides a method for identifying a subject
27 having a nutritional deficiency. The method comprises obtaining an image of the subject's
28 ocular posterior pole; comparing the image to at least one reference ocular posterior pole
29 image; and identifying a nutritional deficiency in the subject based on the comparison to the
30 reference image.

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1 **[0009]** In some embodiments color retinal photographs are converted to grayscale
2 images of the choroid, the retina and the RNFL (retinal nerve fiber layer). The RNFL
3 grayscale images of a subject are compared to reference RNFL grayscale images.

4 **[0010]** In some embodiments, if the reference image is a healthy posterior pole, then an
5 obtained image that comprises at least one region of increased contrast relative to the
6 reference image is indicative of the nutrient deficiency. In some embodiments, if the
7 reference image is a nutrient deficient posterior pole, then an obtained image that comprises
8 at least one region of equal or increased contrast relative to the reference image is indicative
9 of the nutrient deficiency. In some embodiments, the nutrient deficiency comprises a
10 deficiency of one or more of lutein and zeaxanthin.

11 **[0011]** In some embodiments, the method further comprises monitoring a subject for
12 nutritional deficiency. In some embodiments of the monitoring method, a subsequent image
13 is obtained from the subject's posterior pole and compared with an image obtained from the
14 subject at an earlier point in time. In some embodiments, if the subsequent image depicts
15 increased contrast relative to the earlier image, then the subsequent image is indicative of
16 lower nutrient levels in the subject's posterior pole. In some embodiments, if the subsequent
17 image depicts decreased contrast relative to the earlier image, then the subsequent image is
18 indicative of higher nutrient levels in the subject's posterior pole.

19 **[0012]** In some embodiments, the method further comprises assigning a score to the
20 obtained image, wherein the score is based on a comparison between the obtained image
21 and a reference database comprising posterior pole images obtained from a range of
22 nutrient sufficient (healthy) and nutrient deficient subjects, wherein scores at opposite ends
23 of the range are indicative of high nutrient levels (very healthy) and severely nutrient
24 deficient subjects, respectively. In some embodiments, the assigned score is indicative of
25 lutein and zeaxanthin levels in the subject's posterior pole.

26 BRIEF DESCRIPTION OF THE DRAWINGS

27 **[0013]** The features of the invention will become more apparent in the following detailed
28 description in which reference is made to the appended drawings wherein:

29 **[0014]** FIGS. 1A-H are ocular images obtained from glaucoma patients.

30 **[0015]** FIGS. 2A-H are ocular images obtained from geographic atrophy (GA) patients.

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- 1 [0016] FIGS. 3A-L are ocular images obtained from diabetic retinal fibrosis patients.
- 2 [0017] FIGS. 4A-K are ocular images obtained from a patient having retinal RNFL
3 fibrosis.
- 4 [0018] FIGS. 5A-Q are ocular images obtained from wet AMD patients.
- 5 [0019] FIGS. 6A-T are ocular images obtained from VRT patients.
- 6 [0020] FIGS. 7A-H are ocular images obtained from CRVO/BRVO patients.
- 7 [0021] FIGS. 8A-F are ocular images obtained from a pre-retinal detachment patient.
- 8 [0022] FIGS. 9A-D are ocular images depicting reversal of arterial sclerosis of the
9 central retinal arteries.
- 10 [0023] FIGS. 10A-D are ocular images obtained from a subject having presumed arterial
11 sclerosis of the choroidal arteries.
- 12 [0024] FIGS. 11A-D are ocular images obtained from a subject having epiretinal
13 membrane.
- 14 [0025] FIGS. 12A-D are ocular images obtained from a subject having early low-tension
15 glaucoma.
- 16 DETAILED DESCRIPTION OF THE INVENTION
- 17 [0026] The definitions of certain terms as used in this specification are provided below.
18 Unless defined otherwise, all technical and scientific terms used herein generally have the
19 same meaning as commonly understood by one of ordinary skill in the art to which this
20 invention belongs.
- 21 [0027] As used herein, the term "about" will be understood by persons of ordinary skill in
22 the art and will vary to some extent depending upon the context in which it is used. If there
23 are uses of the term which are not clear to persons of ordinary skill in the art, given the
24 context in which it is used, "about" will mean up to plus or minus 10% of the enumerated
25 value.
- 26 [0028] As used herein, the "administration" of an agent to a subject includes any route of
27 introducing or delivering to a subject a compound to perform its intended function.

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1 Administration can be carried out by any suitable route, including orally, sublingually,
2 intraocularly, intranasally, intravenously or topically. Administration includes self-
3 administration and the administration by another.

4 **[0029]** The terms “comprise”, “comprises”, “comprised” or “comprising” may be used in
5 the present description. As used herein (including the specification and/or the claims), these
6 terms are to be interpreted as specifying the presence of the stated features, integers, steps
7 or components, but not as precluding the presence of one or more other feature, integer,
8 step, component or a group thereof as would be apparent to persons having ordinary skill in
9 the relevant art.

10 **[0030]** As used herein the term “end organ” or “EO” refers to a tissue that is supplied by
11 small-diameter arteries and capillaries of that organ, wherein the tissue is the terminal
12 delivery point of a given artery or capillary.

13 **[0031]** As used herein, the term “lesion” refers to a localized change in an organ or
14 tissue of the body. “Retinal lesions”, referred to herein, can be characterized by at least one
15 of puckering, fibrosis or gliosis, lamellar splitting, retinal dragging and/or swelling, bulging of
16 retinal tissues, retinal holes, edema, swelling, exudates, deposits, hemorrhaging and
17 atrophy.

18 **[0032]** As used herein the term “microvascular non-perfusion” or “MVNP” refers to
19 incomplete filling and/or emptying of blood in small-diameter arteries and capillaries.

20 **[0033]** As used herein, the term “nutraceutical” refers to specific chemical compounds
21 found in foods that can prevent disease or ameliorate an undesirable condition.

22 **[0034]** As used herein, the term “nutritional deficiency disorder” refers to an impairment
23 of normal physiological function of any tissue of the eye, wherein the cause of impairment is
24 the lack of one or more nutrients.

25 **[0035]** As used herein, the term “Oculus Dexter” or “OD” refers to the right eye of a
26 subject.

27 **[0036]** As used herein, the term “Oculus Sinister” or “OS” refers to the left eye of a
28 subject.

29 **[0037]** As used herein, the term “omega 3 fatty acids” refers to fats commonly found in
30 marine and plant oils, such as fish oils, algal oil, squid oil, echium oil and flaxseed oil.

1 Examples of omega 3 fatty acids useful in the present invention include, but are not limited
2 to, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).

3 **[0038]** As used herein the term "probiotic" refers to one or more strain of live
4 microorganisms that may confer a health benefit on their host. Probiotics can be consumed
5 as part of fermented foods or as dietary supplements. Examples of probiotic organisms
6 include some members of the Order Lactobacillales, such as *Lactobacillus* spp. And
7 members of the genus *Bifidobacterium*.

8 **[0039]** As used herein, the term "retinal disorder" or "disorder of the retina" refers to any
9 impairment of normal physiological function of the retina.

10 **[0040]** As used herein, the term "therapeutically effective amount" refers to a quantity
11 sufficient to achieve a desired therapeutic and/or prophylactic effect, e.g., an amount which
12 results in the prevention of, or a decrease in, the symptoms associated with a retinal
13 disorder. For example, a "therapeutically effective amount" of the composition of the present
14 invention refers to levels of the composition that, when administered to the subject on a daily
15 basis, ameliorate, in part or in full, at least one symptom of the disorder, for example, the
16 size of a retinal lesion.

17 **[0041]** As used herein, the terms "treating" or "treatment" or "alleviation" refers to both
18 therapeutic treatment and prophylactic or preventative measures, wherein the object is to
19 reverse, prevent or slow down (lessen) the targeted pathologic condition or disorder. A
20 subject is successfully "treated" for an ocular disorder if, after receiving an effective
21 therapeutic amount of the composition according to the methods described herein, the
22 subject shows measurable reduction in at least one symptom or sign of an ocular disorder. It
23 is also to be appreciated that the various modes of treatment or prevention of medical
24 conditions as described are intended to mean "substantial", which includes total but also less
25 than total treatment or prevention, and wherein some biologically or medically relevant result
26 is achieved.

27 **[0042]** As used herein, the terms "units of diameter" and units made in reference to
28 lesion size or diameter refer to units of diameter of the posterior pole of an eye, which
29 measures ten units in diameter between the vascular arcades. A lesion can be larger than
30 10 units.

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- 1 **[0043]** As used herein, the terms "vitreomacular traction," (VMT) and "vitreoretinal
2 traction disorder" (VRTD) refer to conditions wherein the membrane of the vitreous gel of the
3 human eye adheres to the retina, causing pulling, or "traction", forces on the retina that can
4 cause ocular damage.
- 5 **[0044]** Abbreviations and Acronyms
- 6 **[0045]** In addition to the above noted definitions the following abbreviations and
7 acronyms may appear in the application:
- 8 CRA – central retinal artery
- 9 choroid-choriocapillaris
- 10 ONH-optic nerve head
- 11 RPE-retinal pigment epithelium disruption
- 12 GA-Geographic Atrophy (of all retinal layers)
- 13 OU- both eyes
- 14 RTC- return check-up
- 15 IOL- intraocular lens
- 16 CWS- cotton wool spot
- 17 e/d/360/240- dose comprising 360mg of EPA and 240 mg of DHA.
- 18 e/d/180/120- dose comprising 180 mg of EPA and 120mg of DHA
- 19 DD- disc diameter
- 20 ERM- epiretinal membrane
- 21 CSR- central serous retinopathy
- 22 pre-ERM – pre-epiretinal membrane
- 23 pre-CRS- pre- central serous retinopathy
- 24 rpe-retinal pigment epithelium

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1 VA LP- visual acuity of light perception

2 CCA- common carotid artery

3 ICA- internal carotid artery

4 CME- central macular edema

5 CRVO- central retinal vein occlusion

6 BRVO- branch retinal vein occlusion

7 **[0046]** The present invention is based on the inventor's observations of subjects having
8 various ocular diseases. Upon treatment with nutrient supplements, including at least about
9 20 mg lutein and at least about 5 mg zeaxanthin, the inventor observed alleviation of various
10 ocular disorders in the subjects. Further, the inventor began documenting characteristics of
11 the retina and the retinal nerve fiber layer (RNFL) in subject's ocular posterior poles before
12 and after treatment. An emerging trend in these characteristics led the inventor to develop a
13 method of identifying nutrition deficiency disorders (NDDs) in subjects by way of an eye
14 examination.

15 **[0047]** In one aspect of the present invention, a method for identifying a subject having a
16 NDD is provided. The method involves a non-invasive eye examination using a camera,
17 such as a retinal camera, and software capable of imaging the posterior pole of the eye.
18 The skilled artisan is aware of various cameras and software for imaging the posterior pole
19 of the eye, including, but not limited to EyeScape Digital Imaging Software. The image of the
20 subject's posterior pole is then compared to a predetermined reference standard. In some
21 embodiments, the predetermined reference standard is a reference database. The database
22 comprises various photos of posterior poles in subjects having a range of ocular nutrient
23 deficiencies and states of health. Based on the comparison to the reference standard, the
24 image generated is assigned a score. The assigned score may be called a Nutritional
25 Deficiency Score (NDS). In some embodiments, the score is an integer from 1 to 5, wherein
26 1 indicates a healthy eye having good nutritional health and 5 indicates a subject having
27 severe nutrient deficiency. A subject having severe nutrient deficiency, e.g., a score of 4 to
28 5 is typically at high risk for eye disease or is already suffering from eye disease. A subject
29 having a score of three is at lower risk for eye disease but might be prescribed a nutrient
30 composition to prevent development of eye disease. A score of 1 or 2 indicates a healthy
31 eye having good nutritional health. In some embodiments, the scale used to score nutrient

1 deficiency is generally linear rather than exponential or logarithmic, for example. In some
2 embodiments color retinal photographs from the subject are converted to grayscale images
3 of the choroid, the retina and the RNFL (retinal nerve fiber layer). The RNFL grayscale
4 images of a subject are then compared to reference RNFL grayscale images.

5 **[0048]** It is contemplated herein that a reverse numbering scale could be used, in which
6 increased scores over time would indicated improved ocular health and nutrient levels.
7 Further, it is contemplated that non-linear scoring systems could be used to achieve a similar
8 characterization of ocular health and/or nutrient deficiency.

9 **[0049]** In some embodiments of the present invention, the nutrient deficiency is primarily
10 a lutein and zeaxanthin deficiency. In some embodiments a score indicating combined lutein
11 and zeaxanthin sufficiency or deficiency is provided. In some embodiments a score of lutein
12 deficiency is provided. In some embodiments a score of zeaxanthin deficiency is provided.
13 Lutein and zeaxanthin are distributed in different zones of the retina. Lutein deficiencies are
14 identified within the vascular arcades with the exception of the macula itself. Zeaxanthin
15 deficiencies are identified beyond the vascular arcades and in the macula itself.
16 Zeaxanthin collects in the center of the macula while lutein is distributed throughout the rest
17 of the retina.

18 **[0050]** A nutritional deficiency score of zeaxanthin alone would reflect the relative level
19 of pigmentation in the zeaxanthin zone. A nutritional deficiency score of lutein alone would
20 reflect the relative level of pigmentation in the lutein zone. A combined lutein and zeaxanthin
21 nutritional deficiency score would reflect the relative level of pigmentation of the entire retina
22 of a subject.

23 **[0051]** In another aspect of the present invention, a method for treating a nutrient
24 deficiency in a subject is provided. The method involves generating an image of a subject's
25 posterior pole, comparing the generated image to a reference and assigning a score to the
26 generated image based on the comparison. In some embodiments, if the subject's posterior
27 pole image has a score indicative of a nutrient deficiency then the subject is treated with a
28 nutraceutical composition for a period of at least two weeks. In some embodiments, the
29 nutrient deficient subject will be administered daily with at least about 20 mg lutein and at
30 least about 5 mg zeaxanthin. In preferred embodiments, the nutrient deficient subject will be
31 administered daily with at least about 20 mg lutein, at least about 5 mg zeaxanthin, at least
32 about 180mg omega-3 fatty acids (e.g., EPA) and at least about 120 mg DHA. In some
33 embodiments, the nutrient deficient subject will be administered daily following supper

1 comprising protein with "LZO3P" therapy comprising 20 mg lutein, 5 mg zeaxanthin, 180mg
2 EPA omega-3 fatty acids and 120 mg DHA.

3 **[0052]** In some embodiments, the treated subject will have a further eye examination
4 following treatment, wherein a second NDS is generated. Preferably, the second NDS is
5 compared to both the first NDS and the corresponding reference standard(s). In this way,
6 the scores before and following treatment with the nutraceutical composition can be
7 compared. Assuming the 1 to 5 scoring scale discussed above, a decreased score following
8 treatment may accompany an improvement in nutrient sufficiency while an increased score
9 following treatment would indicate a worsening nutrient deficiency. Assuming the 1 to 5
10 scoring scale discussed above, a decreased score following treatment would further indicate
11 an improvement in ocular health while an increased score following treatment would indicate
12 a worsening ocular health.

13 **[0053]** In some embodiments of the present invention, the composition is administered
14 to the subject orally. The compositions of the invention can be formulated with suitable
15 carriers such as starch, sucrose or lactose in tablets, capsules, solutions, powders, syrups
16 and emulsions, or oils. Suitable optional carriers include but are not limited to, for example,
17 fatty acids, esters and salts thereof, that can be derived from any source, such as for
18 example, natural or synthetic oils, fats, waxes or combinations thereof. In preferred
19 embodiments of the present invention, the source of the fatty acids is DHA and EPA, which
20 may be provided in combination with the composition or separately.

21 **[0054]** In some embodiments of the present invention, the composition is administered
22 daily for two to 24 months to the subject. In preferred embodiments, the composition is
23 administered daily to the subject for 3 months. In particularly preferred embodiments of the
24 present invention, the composition is administered to the subject daily until ocular disease(s)
25 are ameliorated completely and/or the subject has an NDS of 1, 2 or 3.

26 **[0055]** In another aspect of the present invention, a method for monitoring a nutrient
27 deficiency in a subject is provided. In some embodiments, the method of monitoring
28 involves repeatedly obtaining nutritional deficiency scores from a subject over time, using the
29 method disclosed above. Repeated measurements can allow comparison to previous states
30 of eye health and/or disease and to a reference. Further, repeated measurements can allow
31 evaluation of various treatments for eye health and disease.

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1 **[0056]** It is contemplated herein that the present methods of treating and monitoring
2 nutrient deficiencies, can be useful for improving various ocular disorders, including, but not
3 limited to, one or more of AMD, (dry and wet), vitreoretinal traction disorder (VRTD), central
4 macular edema, CME, diabetic macular edema, DME, diabetic retinopathy, retinal
5 hemorrhages, sub-choroidal hemorrhages, cotton wool spots, retinal exudates, low-tension
6 glaucoma, cataract, open angle glaucoma, miosis, iris edema, angle closure glaucoma,
7 corneal dystrophy, corneal guttata, pterygia secondary to xerophthalmia, meibomian gland
8 dysfunction, recurrent eyelid styes, recurrent chalazia, severe dry eye, and eyelid ectropion.
9 Diagnosis can be made using methods known to those of skill in the art, at least for example,
10 slit lamp biomicroscopy, retinal photography, visual acuity, Amsler grid intraocular pressure,
11 central corneal thickness or fundus examination.

12 **[0057]** Without being bound to any one theory, it is contemplated herein that the nutrient
13 deficiency that is characterized by a darkening of at least a portion of the RNFL of a
14 subject's eye is associated with microvascular non-perfusion. It is contemplated that
15 microvascular nonperfusion limits blood flow and, consequently limits nutrient delivery to and
16 waste removal from end organ locations, such as the eye. It is contemplated that
17 microvascular nonperfusion-associated darkening of a subject's posterior pole might be
18 otherwise asymptomatic. It is contemplated that reversal of microvascular nonperfusion, for
19 example by way of nutrient therapy, might prevent or reverse various eye diseases.

20 **[0058]** It is contemplated herein that unilateral eye disease may occur secondarily to
21 asymptomatic carotid stenosis and that one or more of the internal, external and common
22 carotid arteries may be involved. It is contemplated herein that internal carotid stenosis can
23 result in one or more of the following: AMD, (dry and wet), VRTD, central macular edema,
24 diabetic macular edema, diabetic retinopathy, retinal hemorrhages, sub-choroidal
25 hemorrhages, cotton wool spots, retinal exudates, low-tension glaucoma, mini-BRVO,
26 cataract, open angle glaucoma, miosis, iris edema, angle closure glaucoma, corneal
27 dystrophy, corneal guttata, pterygia secondary to xerophthalmia, meibomian gland
28 dysfunction, recurrent eyelid styes, recurrent chalazia, severe dry eye, and eyelid ectropion.
29 It is contemplated that external carotid stenosis can result in one or more of the following:
30 reduced lacrimal and salivary gland secretions, meibomian gland dysfunction, recurrent
31 eyelid styes, recurrent chalazia, severe dry eye and eyelid ectropion.

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1 [0059] EXAMPLES

2 [0060] The present invention is further illustrated by the following examples, which
3 should not be construed as limiting in any way.

4 [0061] Example 1: Materials and methods

5 [0062] Imaging of subject posterior poles: retinal photographs were taken using a Canon
6 CR-1 Digital Retinal Camera and analyzed using EyeScape Digital Imaging Software,
7 version 7.5.5.

8 [0063] The settings used for taking retinal photographs were such that optimal contrast
9 and brightness for each subject was achieved. Most retinal photographs were taken with a
10 dilated pupil. Some subjects have naturally very large pupils. In these cases, pupil dilation
11 may not have been required to obtain sufficient images. The Canon CR-1 has a setting for
12 small pupils that was used as required.

13 [0064] Determination of retinal lesion size: Retinal photographs were examined for signs
14 of ocular disease. VRTD lesion size was measured directly from the computer screen
15 display of a subject's retinal photograph. One "unit" was equivalent to one tenth of the
16 diameter of the posterior pole, within the vascular arcades.

17 [0065] Recording of other health characteristics: non-ocular health conditions were, in
18 some cases, reported by subjects. These conditions were recorded.

19 [0066] Nutrient supplements and administration protocol:

20 [0067] Example 2: Retinal photograph analysis indicated a positive correlation between
21 VRTDs and high NDSs and lutein and zeaxanthin treatment resulted in decreased NDS and
22 lesion size.

23 [0068] Subject Description: Data were collected from 40 subjects having asymptomatic
24 or symptomatic VRTD over a period of 4.5 years.

25 [0069] Treatment: Subjects were treated daily with lutein and zeaxanthin as described
26 in table 1. Nutritional deficiency scores (NDSs) and lesion sizes were measured at various
27 time points. The nutritional deficiency scoring rubric involves a scoring system of 1 to 5,
28 wherein 1 indicates a healthy eye having sufficient lutein and zeaxanthin and 5 indicates a

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1 severely nutrient deficient eye, wherein lutein and zeaxanthin levels are low relative to a
2 healthy eye and correlate with ocular disease.

3 **[0070]** Table 1: Raw data collected from subjects during preliminary lutein zeaxanthin
4 trial. Combined Lutein (L) and Zeaxanthin (Z) NDSs are provided for each eye (OD and OS).
5 Plh indicates partial lamellar hole. Pucker (macular) is described based on a qualitative
6 score of mild to severe, wherein a score of 1 of 3 is a mild pucker, a score of 2 of 3 is a
7 moderate pucker and a score of 3 of 3 is a severe pucker.

Case #	M/F	DOB	Exam Date	lutein (mg)	Zeaxanthin (mg)	OD NDS	OD lesion	OS NDS	OS lesion	Comments
730 1	M	1939	Jul-08	0	0			1.5	6	NAD = normal
			Oct-09	10	2	2	0.5	2	5	Self-treated
			Nov-12	0	0	3	4.5	4	8	non-compliance
			Nov-11	10	2	2	2	2	4	complied
			May-12	20	5	n/a	0.5	n/a	0	increased dose
			Oct-12			2	0.5	2	0	
402 2	F	1959	Apr-09	0	0	2	0	2	8.5	
			Nov-10	20	0	3	0	3	3	
			Mar-12	20	5	4	0	4	0	
			Sep-12	0	0	n/a	1	n/a	0.5	regression next 5.7/1.4
378 3	M	1959	May-10	0	0	4	9	4	0	
			Jun-11	0	0	4	11.5	4	0	
			Dec-11	2.5	0.625	3	10	4	0	
			Sep-12	0	0	4	14	4	0	
			Feb-13	20	5	4	14	4	0	cont.20/5
1562 4	F	1951	Aug-10	0	0	3	5	3	0	
			Jul-12	0	0	3	5	3	0	
			Mar-13	20	5	4	4	3	0	multi strain probiotic next
1556 5	F	1941	Jul-10	0	0	2	4.5	2	11.5	
			Jan-11	5	1	3	4	2	12	
			Aug-11	20	0.8	4	7	2	12	
			Aug-12	20	0.8	3	6.5	3	11.5	Next 20/5-no rtc yet
1895 6	M	1950	Feb-11	0	0	4	7	4	7	
			Aug-11	20	5	3	6.5	3	7	
			Jul-12	20	5	3	4	3	7	slow or non- responder-no rtc yet – probiotics next?
1997 7	F	1958	May-11	0	0	2	5	2	0	
			Nov-11	0	0	4	8	4	0	
			May-12	0	0	3	8.5	3	0	Next 20/5- no rtc yet
294 9	M	1928	Jan-11	10	0.5	4	11.5	4	0.5	AMD OD/ IOL OU
			Jul-11	10	0.5	3	7.5	3	0.5	
			Jan-12	30	1.3	3	8.5	3	0.5	
			Aug-12	25	1.05	5	7.5	3	0.5	
			Feb-13	30	5.5	3	7	3	8	right stenosis reversed

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Case #	M/F	DOB	Exam Date	lutein (mg)	Zeaxanthin (mg)	OD NDS	OD lesion	OS NDS	OS lesion	Comments
1132 10	F	1949	Jan-10	0	0	3	5.5	3	1.5	
			Jul-10	0	0	2	8.5	3	3.5	
			Jan-11	5	1	4	8.5	4	5.5	cancelled rtc
1660 11	F	1945	Oct-10	0	0	4	7.5	4	0	
			Apr-11	0	0	4	7.5	3	0	
			Oct-11	0	0	3	7.5	3	0	
			Apr-12	20	5	4	8	4	0	more meat/less fish/next more fish less meat advised/20/5
			Apr-13	20	0	4	7	2	0	no Z=continued right carotid stenosis, next 20/5
2010 12	F	1945	May-11	10	2	4	5.5	4	12	AMD OU
			Dec-11	10	2	3	11	5	11.5	
			Jul-12	22.5	5.5	3	0	2	13.5	
			Jan-13	5	0.25	4	4	3	6	Increase drusen OU
483 13	M	1931	Apr-10	0	0	3	8.5	3	0.5	
			May-11	0	0	4	9.5	4	0	
			Nov-11	0	0	4	9	5	0	took 1 bottle 10/2.5 before nov-11
			May-12	18	0	3	0	4	0	
1423 14	M	1946	May-10	0	0	2	0.5	2	0	
			May-12	0	0	3	12	2	0	2 years later/refuses 20/5 Refuses 20/5 bilateral stenosis?
			Nov-12	0	0	4	12	4	0	
353 15	F	1934	Mar-09	0	0	2	8.5	2	9	
			Apr-10	10	0.5	2	10	2	11	AMD OU
			May-11	7.5	0.37	3	9.5	3	8.5	
			May-12	5	1	3	9.5	3	9	next 20/5 Mental confusion=wrong dose=still no improvement =start probiotics
			Dec-13	60	15	4	9.5	3	9.5	=start probiotics 20/5 & probiotics reverse od VRT and right stenosis
1688 16	F	1949	Dec-13	0	0	3	0	3	0	
			Apr-13	0	0	3	0	4	13.5	
			Oct-12	20	5	2	11.5	3	14.5	
			Nov-13	20	5	3	10	4	9.5	probiotics started
1274 17	M	1941	Mar-10	0	0	4	7.5	4	0.5	
			Sep-10	0	0	1	6.5	1	0.5	cancer/started taking many supplements/no lutein/no zeaxanthin
			Apr-11	0	0	2	0	3	0	
			Sep-11	0	0	2	0.5	4	0	Cancelled 04/12 -left stenosis
242 18	M	1943	Feb-09	0	0	2	6.5	2	9.5	
			Jul-10	0	0	3	6.5	3	10.5	
			Jan-11	10	2	3	6.5	3	9.5	

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Case #	M/F	DOB	Exam Date	lutein (mg)	Zeaxanthin (mg)	OD NDS	OD lesion	OS NDS	OS lesion	Comments
			Jul-11	10	2	3	2	2	8.5	
			Jan-12	10	2	4	0.5	4	8	
			Jun-12	20	5	4	0.5	4	8	cont.20/5
			Dec-13	20	5	4	0.5	4	4	probiotics started
			Mar-13	20	5	3	0	3	0.5	
895 19	M	1941	Sep-08	0	0		0		0	no photos until Nov, 2009
			Sep-09	0	0	1	0.5	2	0	OS heme
			Jan-10	0	0	2	0.5	3	0.5	diabetic
			Sep-10	0	0	2	0	4	7.5	
			Oct-11	10	2	1	0	4	8.5	
			Apr-12	20	5	1	0	2	0.5	used only 2 months- reversed left VRT, diabetes and left stenosis
			Oct-12	20	5	1	0	1	0.5	gall bladder surgery
			Apr-13	20	5	1	0	1	0	
615 20	F	1944	Jun-09	10	0.5	1	0.5	0	0	OS AMD
			Dec-09	10	0.5	4	0	4	0	
			Jun-10	5	0.25	3	10.5	3	0	
			Dec-10	5	0.25	4	8	4	0	
			Jul-12	5	0.25	4	0.5	4	0	
			Apr-13	20	5	2	0	2	0	
619 21	F	1948	Jun-09	0	0	3	0	3	11	
			Jun-11	20	0.8	3	0	3	8.5	
			Feb-12	20	0.8	1	0.5	2	7.5	next 20/5
			Sep-12	20	0.8	2	0.5	3	7.5	
			Apr-13	20	5	4	0	3	8	needs probiotics
181 22	F	1926	Jan-09	0	0	1	0	1	0	IOL OU, OS 1 CWS
			Sep-09	2.5	0.125	1	4	1	0	CME OU, using unknown product
			Feb-10	0	0	2	4	2	0	
			Apr-11	5	1	1	4.5	1	0	next 20/5
127 23	F	1946	Mar-10	0	0	3	0.5	4	0	OS drusen
			Oct-10	0	0	3	8	4	0	
			Apr-11	0	0	3	7	3	0	e/d/360/240
			Nov-11	20	5	3	6.5	3	0	e/d/180/120
			Apr-12	20	5	3	0.5	3	0	drusen gone/e/d/180/120
2038 24	F	1954	Jun-11	0	0	3	11.5	2	0	
			Dec-11	20	5	3	8.5	2	0	e/d/360/240 e/d360/240 slow responder/compliance?
			Jul-12	20	5	3	6	3	0	Left stenosis, needs probiotics
			Jan-13	20	5	3	5	4	0	
725 25	M	1949	Jul-09	0	0	n/a	?	3	0	e/d/180/120 e/d/360/240 right stenosis caused cataract, then severe ERM OD only
			Mar-12	0	0	5	12	3	0	

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Case #	M/F	DOB	Exam Date	lutein (mg)	Zeaxanthin (mg)	OD NDS	OD lesion	OS NDS	OS lesion	Comments
1343	M	1929	Apr-10	0	0	2	4.5	2	2	OS macular drusen 1/3 DD size
26			Apr-11	10	0.5	3	4	2	0	OS macular drusen 1/3 DD size, now 1/2 resolved in retina layer
			Oct-11	10	2.5	2	0	1	0	OS macular drusen 1/3 DD size, now 90% resolved in retina layer
			Apr-13	10	2.5	3	0	1	0	right stenosis reversed OS macular drusen, now getting worse with stenosis of blood supply
			Jan-13	10	0	3	0	3	0	OU
74	F	1951	Dec-08	0	0	3	0.5	3	0.5	
27			Jan-10	5	0.25	3	0.5	3	0.5	e/d180/120
			Jul-10	5	0.25	3	2	3	2	e/d/180/120
			Mar-11	5	0.25	4	7.5	4	6.5	e/d/180/120
			Dec-11	5	0.25	3	5	3	8.5	no e/d
			Jul-12	20	0.8	2	4	2	8	e/d180/120 high stress levels, needs rtc
			Feb-13	20	5	4	0.5	4	8	
224	M	1941	Jun-10	0	0	n/a	1	n/a	0.5	
28			Nov-11	0	0	2	10.5	2	8.5	
			May-12	20	5	2	9.5	2	8.5	e/d/360/240 only took one bottle, ret. spec. Said "throw them away"
			Dec-12	20	5	2	5	2	4.5	e/d/360/240
686	M	1930	Oct-07	0	0	n/a	0	n/a	0	vague decrease vision OD
29			Jul-09	0	0	1	0	2	0	
			Jun-11	0	0	2	0	2	0	OD moderate pucker, va 20/40
			Dec-11	0	0	2	0	2	0	OD moderate pucker, va 20/40
			Jun-12	20	5	3	0	3	0	OD mild pucker, va 20/25
			Dec-12	20	5	2	0	2	0	OD mild pucker, va 20/25
			Apr-13	20	0.8	2	0	2	0	
689	M	1948	Jul-09	0	0		9			only has one eye
30			Oct-09	5	0.25	2	10			
			Oct-09	5	0.25	2	10.5			
			Dec-09	10	0.5	4	10.5			e/d/360/240
			Apr-12	5	0.25	4	11.5			*plh 4 mm e/d/360/240 4 mon. later*plh 2mm, e/d/360/240
			Aug-12	20	5	3	10.5			
			Feb-13	0	0	3	10.5			
763	M	1951	Aug-09	0	0	3	0	3	5.5	
31			Sep-10	0	0	3	0	4	5.5	e/d/180/120
			Aug-12	5	0	4	0	4	0.5	23 mon later, inc fish/chicken, dec beef
150	M	1951	Feb-10	0	0	4	0	4	0	

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Case #	M/F	DOB	Exam Date	lutein (mg)	Zeaxanthin (mg)	OD NDS	OD lesion	OS NDS	OS lesion	Comments
32			Sep-11	0	0	4	11	4	0	e/d/180/120
			Mar-12	20	5	3	5.5	3	0	
			Sep-12	20	5	3	5.5	3	0	inc. BFV
879 33	F	1946	Sep-10	0	0	4	0	4	0.5	e/d/540/360
			Sep-11	0	0	4	0	4	0.5	e/d/180/120
			Mar-12	20	5	3	0	3	0	e/d/360/240
			Sep-12	20	5	4	0	4	0	e/d/360/240
131 34	F	1937	Jan-09	0	0	1	0.5	1	12	
			Jan-10	0	0	2	0	1	13	
			Nov-10	0	0	2	0	n/a	15.5	e/d/360/240
			Jun-11	10	2	3	0	2	15	e/d/360/240
			Feb-12	10	2	2	0	2	6.4	
			Aug-12	10	2	2	0	2	3.8	
1774 35	M	1930	Jun-07	0	0		0.5		0	next visit 41 mon.no photos yet
			Nov-10	0	0	3	12	3	0	IOL OU now
			Jun-11	10	0	4	9.5	4	0	e/d/180/120
			Aug-12	10	0	3	4.5	3	0	14 mon using garlic, cinnamon, hot pepper, lemon, honey
			Feb-13	0	0	3	4.5	4	0	
1662 36	F	1954	Sep-08	0	0					od plh, no photos yet
			Oct-10	0	0	4	11.5	4	9	od plh 8x5 mm.
			Aug-12	5	1	3	11	3	6	e/d/360/240 plh 8x5mm
			Feb-13	20	5	5	9	4	0	
630 37	M	1946	Jun-09	0	0	3	0	2	0	23 years diab.
			Jun-10	0	0	4	0	4	0.5	
			Jun-11	0	0	4+	0.5	4+	1	
			Jul-12	0	0	3	0	3	9	
			Mar-13	10	2.5	3	0	3	7	worse, advised L 20 and Z5
1010 38	F	1954	Jan-10	0	0	3	0	4	4.3	OS "central red 'scotoma'" va 7.5- plh 10 mm
			Jan-12	0	0	3	0	4	8	N/A plh mm
			Jul-12	20	5	1	0	2	0	Plh 5 mm worse, advised L 20 and Z5 Plh 4 mm
			Mar-13	10	2.5	2	0	3	9	
1011 39	M	1942	Nov-09	0	0	2	0	2	0	Intermediate AMD OU
			May-10	10	2	3	0	3	0	e/d/360/240
			Aug-10	10	2	4	10.5	4	2.5	e/d/720/480
			Nov-10	10	2	3	9.5	3	2.5	e/d/360/240
			Jan-13	20	5	4	8	3	2	
			Apr-13	20	5	2	4	3	1.5	ERM resolving on 20/5, AMD stable
1151 40	F	1957	Jan-10	0	0	3	6.4	3	0	od drusen and ERM started L10, Z2 for drusen
			Jul-10	10	2	4	5.1	3	0	e/d/360/240
			Jan-11	10	2	4	4.6	4	0	e/d/360/240

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Case #	M/F	DOB	Exam Date	lutein (mg)	Zeaxanthin (mg)	OD NDS	OD lesion	OS NDS	OS lesion	Comments
			Jul-11	10	2	3	4.3	3	0	e/d/360/240 ERM peeling off!
			Feb-12	10	2	4	3.2	4	0	e/d/360/240 ERM peeling off!
			Mar-12	10	2	4	2.7	4	0	e/d/360/240

1

2 **[0071]** Results: Treatment of retinal lesions with some combination of lutein and
3 zeaxanthin was useful for decreasing subject's NDS's and ameliorating and decreasing the
4 size of retinal lesions in subjects having VRT. Frequently, when patients stopped or reduced
5 their dosage their NDS increased and ocular disease recurred. It is contemplated that
6 unilaterally increased NDS and unilateral eye disease may be due to unilateral carotid
7 stenosis.

8 **[0072]** Daily oral administration to a subject of 10-20 mg lutein and 0.5-5 mg zeaxanthin
9 was sufficient to decrease NDS and retinal lesions in the majority of subjects who had not
10 previously been treated with lutein and/or zeaxanthin. Some patients were on low doses of
11 lutein and zeaxanthin for AMD and still developed VRTD. Increased doses of lutein and
12 zeaxanthin were required to reverse VRTD.

13 **[0073]** Example 3: LZO3P dosage response trials indicate positive results for treatment
14 ocular health and nutrient deficiency as indicated by decreased nutritional deficiency scores
15 and improvement in various ocular symptoms.

16 **[0074]** Subject Description: Data were collected from 41 subjects having various states
17 of ocular health at a first time point and a second time point and optionally a third time point,
18 the second time point being three months after the first and the third time point being three
19 months after the second. Treatment was started after the first time point.

20 **[0075]** Treatment: Subjects were treated daily with the LZO3P composition (i.e., lutein
21 (20 mg) zeaxanthin (5 mg), omega-3 fatty acids (180 mg) and DHA (120 mg)) following an
22 evening meal comprising protein. Nutritional deficiency scores (NDS) and lesion sizes were
23 measured prior to and following 3, and optionally 6, months of treatment. The nutritional
24 deficiency scoring rubric used involved a scoring system of 1 to 5, wherein 1 indicates a
25 healthy eye having sufficient nutrients and 5 indicates a severely nutrient deficient eye,
26 wherein nutrient levels are low relative to a healthy eye and indicative of ocular disease or a
27 likelihood of developing eye disease. In this study, subject ocular lutein and zeaxanthin

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1 levels were scored separately. In some instances a score for elevated retina and/or RNFL
 2 was included under the heading "3-D". A 3-D score of 1 indicates normal 3-D appearance; 2
 3 is moderately abnormal 3-D appearance; 3 is very abnormal 3-D appearance; 5 indicates the
 4 presence of a partial lamellar hole; and 8 indicates the presence of edema.

5 [0076] Table 2: Raw data collected from subjects during 3-month LZO3P trial. Separate
 6 lutein (L) and zeaxanthin (Z) and 3-D ocular health score are provided for both eyes (OD and
 7 OS).

Case #	gender	age	OD L NDS	OD Z NDS	OS L NDS	OS Z NDS	OD 3D	OS 3D	Comment
2093	1	51	3 3.5	3 3	3 3.5	3 3	Pre-erm Pre-erm	Pre-erm Pre-erm	Non-responder
471	1	68	3 2	2 1	3 4	2 3	2 2	2 2	OS rpe Early left carotid stenosis?
2534	1	22	3 2	4 3	3 3	3 3	pre-csr pre-csr	pre-csr pre-csr	No improvement in OS Early left carotid stenosis?
387	1	58	4 3	3 2	4 3	3 2	1 1	1 1	successful prevention
470	1	67	2 1	3 1	4 2	3 1	Od plh 1	OS pucker 1	mild left stenosis, od plh and OS pucker resolved in 3 months!
1804	1	74	3 4	3 4	2 3	1 3	1 1	3 2	OD iol, OU mild drusen & trace erm, OS macular edema OU drusen no change. Con'd Erm and edema gone. Needs M.D. referral for stenosis, maybe probiotics if -ve stenosis
717	1	64	5 2	5 2	4 2	3 2	2 3	2 3	od GA OD dec. fibrosis and dec. excavation of RNFL
2366	1	85	3 2	3 2	2 3	3 3	2 2	2 3	Ou AMD, OD micro plh 6 month trial, no L/ Z/ omega previous 2 weeks, mild left stenosis
2616	1	49	4 2	4 2	4 3	3 3	1 1	1 1	successful prevention
1492	2	46	3 2	3 2	2 3	2 3	1 1	1 1	Diabetes, 1 micro aneurysm Early left carotid stenosis? 0 micro aneurysm
526	1	64	4 2	4 2	4 2	4 2	2 1	2 1	

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Case #	gender	age	OD L NDS	OD Z NDS	OS L NDS	OS Z NDS	OD 3D	OS 3D	Comment
			3	3	3	3	2	2	Recent increased stress in severely stressful life situations
2495	2	65	5	5	3	3	2	2	OD small drusen right stenosis and needs probiotics? (slow response)
			4.5	4.5	2.5	2.5	1	1	
			4	4	2	2	1	1	
2169	2	55	3	3	3	3	3	3	
			2	2	3	3	2	2	
			2	3	2	2	2	2	successful prevention
2266	1	58	3	3	3	3	2	2	
			2	2	2	2	1	2	successful prevention
2169	2	55	3	3	3	3	3	3	
			2	2	3	3	2	2	
			2	2	2	2	1	2	successful prevention
2643	1	60	3	3	4	3	1	1	
			2	1	2	1	1	1	successful prevention, 3-d retina layer now flat OU
1011	1	70	4	2	4	2	1	1	OU AMD, OD pucker, L 10, Z 2 before trials
			3	1	3	2	1	1	
			2	1	2	2	1	1	pucker gone, AMD same
1081	1	68	3.5	2	3	2	1	1	
			2	1	2	1	1	1	successful prevention, 3-d retina layer now flat OU
747	1	62	3	3	3	3	3	3	
			1	1	1	1	1	2	successful prevention
2161	2	53	4	3	3	2	2	1	OD amblyopia, OS macular drusen, L 10, Z 2 before trials
			3.5	2	4	2	2	1	
			3	2	3	2	1	2	slow improvement, OS drusen no change
481	1	74	4	2	4	2	1	1	
			2	2	2	2	1	2	successful prevention
1202	2	73	4	2	3.5	2	1	1	
			2	2	2	2	1	2	successful prevention
1441	1	49	3	3	3	2	3	3	
			2.5	3	3.5	3	3	3	did not use 180/120, Early left carotid stenosis?
93	1	64	2	2	4	4	1	1	od drusen
			3	3	3	3	1	1	right stenosis
718	1	75	3	2	2	4	1	2	06/10 OS (erm) vitrectomy, IOL, OU small plh & severe dry eye, 5 month trial, OU plh smaller & eyelid margins no longer red, left
			2	1	3	3	1	2	

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Case #	gender	age	OD L NDS	OD Z NDS	OS L NDS	OS Z NDS	OD 3D	OS 3D	Comment
									stenosis? (mid-Nov. 2012 \$1500 heat and squeeze eyelid therapy)
2411	1	44	3	3	2	2	2	2	sig. GI probs. Also took probiotics lactose intolerance gone, left stenosis? Reg. Bms, no gas, inc. energy.
			2	2	3	3	2	2	
1784	2	62	3	3	2	3	3	8	left stenosis? OS edema gone
			2	2	3	4	2	3	
2595	1	41	2	2	2	2	2	8	OU Pre-csr
			3	4	3	3	3	3	OS edema gone
1431	1	75	3	3	3	3	1	1	OU AMD & mac. Nevi (nevi, no change x 3 years) OU stenosis. Referred to MD
			5	5	5	5	1	1	
1432	2	80	2	2	2	2	1	8	OS edema
			2	2	1	1	1	1	OS edema gone
459	2	64	4	4	4	3	1	2	OD amblyopia, OS macular drusen, L 10, Z 2 before trials
			2	2	3	2	1	2	successful prevention
353	1	79	2	2	2	2	2	3	OS erm, 7 month trial probiotics added 5 month trial
			3	2	3	2	1	2	no change OS erm, left stenosis?
			2	2	3.5	2	1	2	
615	1	68	4	3	4	3	3	1	
			2	2	2	2	1	1	successful prevention
1456	2	69	4	4	3	3	8	2	OU iol, OD RNFL edema OS cws, refer to MD for hypertension
			3	3	2	2	8	1	
2578	2	67	3	2	3	2	1	1	
			2	2	2	2	1	1	successful prevention
2579	2	66	3	2	3	2	1	1	
			3	2	3	2	1	1	Non-responder
2542	1	50	4	4	3	4	3	3	probiotics also GI more regular, watch OS L
			3	2	4	3	2	2	
865	1	71	3	2	4	3	1	3	arcade ends poorly perfused only OS L and 3-d improved
			3	2	4	2	1	1	
2562	1	70	3.5	4	3	1	3	1	OD iol
			3	3	2	1	1	1	"better distance vision"
955	2	60	4	3	4	3	1	1	sig. GI probs. Also took probiotics
			3	2	2	1	1	1	Improved facial rosacea,

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Case #	gender	age	OD L NDS	OD Z NDS	OS L NDS	OS Z NDS	OD 3D	OS 3D	Comment
									virus recovery now 2-3 weeks instead of 4 weeks
78	1	71	4	3	4	3	1	5	OU erm, OS plh
			2	1	2	1	1	1	Alzheimer's no change

1

2 **[0077]** Results: Treatment of subject with LZO3P was useful for decreasing subject's
3 NDSs (Table 2). In some cases, Lutein NDS and Zeaxanthin NDS differ in the same eye
4 (Table 2). In a review of 8 patients from table 1, zeaxanthin NDSs vs VRT reversal shows
5 that 0.8 zeaxanthin, "Z", was not enough to reverse VRT or to substantially improve Z NDSs.
6 An amount of about 5.0 mg of Z is preferred to reverse microvascular non-perfusion and
7 VRT and to improve Z ND scores. More rapid and greater improvement (reduction in lesion
8 size) occurred when Z was 5.0 mg.

9 **[0078]** Example 4. Treatment of subjects having lutein and zeaxanthin deficiencies with
10 LZO3P can improve NDS and glaucoma.

11 **[0079]** Low tension glaucoma (LTG) is a condition wherein optic nerve head (ONH)
12 degeneration develops despite normal intraocular pressure. It is contemplated that LTG
13 occurs due to MVNP of the ONH. In some cases, lutein and the zeaxanthin NDS (Z NDS)
14 differ in the same eye. In a review of 8 patients from table 1, 5.0 mg of Z was found to
15 reverse microvascular non-perfusion and VRT and to improve Z NDS.

16 **[0080]** Subject Description: Patient 2740 is an 85 year old female. Upon examination on
17 April 29, 2013, the patient had a lutein NDS of 3+ and a zeaxanthin NDS of 5+ in both eyes.
18 It is contemplated that the poor Z NDS is correlated with poor vascular perfusion. OD IOP
19 (intraocular pressure) 14 CCT (central corneal thickness) 516, normal cupping (FIG. 1A); OS
20 IOP 14 CCT 521, inferior notching, probable early LTG (FIG. 1B).

21 **[0081]** Treatment 1: Additional glaucoma testing recommended and LZO3P therapy
22 started.

23 **[0082]** Subject Description: Patient 1061 is a 67 year old male who had asymmetric
24 chronic glaucoma. Prior to LZO3P treatment, on June 3, 2011, patient 1061 had an OD
25 NDS of 5+, retinal detachment, intraocular lens, and end stage glaucoma with severe
26 glaucomatous loss (FIG. 1C). Patient's OS had an average NDS of 3 with moderate and
27 stable glaucomatous loss (FIG. 1D).

- 1 [0083] Prior to treatment, on September 21, 2012 the subject's inferior OS cupping had
2 increased as did OS NDS. OD had an NDS of 5+ (FIG. 1E) and OS had an NDS of 4 (FIG.
3 1F).
- 4 [0084] Treatment 2: LZO3P daily treatment (patient was receiving standard glaucoma
5 treatment as well).
- 6 [0085] Following 5-months LZO3P treatment, glaucoma and nutrient deficiency in the
7 patient's OD remained severe (NDS = 4) (FIG. 1G). However, OS cupping appeared to be
8 stabilizing and OS NDS had improved to 2 (FIG. 1H). It is hypothesized that the NDS
9 improvement observed in the patient's OS indicated reversal of end organ microvascular
10 non-perfusion and stabilization of ocular disease.
- 11 [0086] Example 5. LZO3P treatment of subjects having lutein and zeaxanthin
12 deficiencies can improve geographic atrophy.
- 13 [0087] Geographic Atrophy: patients having end stage AMD, wherein all three layers of
14 the retina scar and/or disappear.
- 15 [0088] Subject Description: Patient 252 is an 86 year old female who had fibrosis,
16 excavation and VA LP OU in both eyes (i.e., vision comprising only light perception; lacking
17 detailed vision). It is contemplated that this patient had severe MVNP in both eyes. On
18 November 19, 2012 the patient had an OU NDS of 5 (OD before and after treatment, FIG.
19 2A and C; OS before and after treatment, FIG 2B and D).
- 20 [0089] Treatment: 4 months of continued LZO3P therapy.
- 21 [0090] Results: Upon examination on March 18, 2013, following four months LZO3P
22 treatment, the patient had an OU NDS of 3, choroidal blood vessels had increased in
23 diameter, fibrosis reversal was observed, excavation was reduced and it is contemplated
24 that MVNP had reversed (OD before and after treatment, FIGS. 2E and G; OS before and
25 after treatment, FIGS. 2F and H).
- 26 [0091] Example 6. LZO3P treatment of subjects having lutein and zeaxanthin
27 deficiencies can improve diabetic retinal fibrosis.
- 28 [0092] Subject Description: Patient 1010 is a 66 year old female who has had diabetes
29 for 23 years. Upon examination on January 26, 2012 the patient exhibited mild retina RNFL
30 fibrosis of the left eye inferior arcade (FIG. 3A)

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- 1 **[0093]** Treatment 1: Lutein (20mg) and zeaxanthin (5 mg) daily.
- 2 **[0094]** Results: Following six months treatment, the patient's mild retina/RNFL and
3 fibrosis were reversed (FIG. 3B).
- 4 **[0095]** Treatment 2: Lutein (20mg) and zeaxanthin (5 mg) every other day.
- 5 **[0096]** Results: Following 6 months on lutein 20mg and zeaxanthin 5 mg every other
6 day, mild retina and RNFL fibrosis returned (FIG. 3C).
- 7 **[0097]** Subject Description: Patient 1625, a 79 year old male with diabetes for 25 years,
8 suffered kidney failure and 6 resuscitations in 2011. Upon examination on June 30, 2011,
9 the patient's OD exhibited severe RNFL fibrosis and had an OD NDS of 4 (FIG. 3D) and the
10 patient's OS exhibited moderate RNFL fibrosis, partial lamellar hole and had an NDS of 5
11 (FIG. 3F).
- 12 **[0098]** Treatment: Daily LZO3P treatment.
- 13 **[0099]** Results: Upon examination on April 23, 2012, following 10 months treatment, the
14 severe OD fibrosis was not reversed despite treatment (FIG. 3F), however the patient's OD
15 NDS had been reduced to 2 (FIG. 3F). RNFL fibrosis was improved in the patient's OS
16 (FIG. 3G) and the patient's OS NDS had been reduced to 3 (FIG. 3G).
- 17 **[00100]** Following 17 months daily LZO3P treatment (December 5, 2012), the patient
18 exhibited an OD NDS of 2 (FIG. 3H) and OS RNFL fibrosis with an NDS of 4 (FIG. 3I). Given
19 the increase of the patient's OS NDS and lack of improvement in the patient's OS fibrosis, it
20 is contemplated that the patient had developed stenosis of his left carotid artery.
- 21 **[00101]** Upon examination on June 3, 2013, following an additional 6 months of daily
22 LZO3P therapy, the patient's OD had an NDS of 2 (FIG. 3J) and an OS NDS of 3 (FIGS. 3K
23 and L). Further, the patient's OS probable left carotid stenosis appeared to be reduced and
24 the OS partial lamellar hole had improved along with improved visual acuity to 20/30.
- 25 **[00102]** Best corrected visual acuity, BCVA, is a measure of ocular health. BCVA of
26 20/50 is required to obtain a driver's license in many jurisdictions.
- 27 **[00103]** Date/ OD BCVA/ OS BCVA
- 28 **[00104]** June 2011/ 20/70 / 20/40

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1 [00105] April 2012/ 20/70 / 20/40

2 [00106] December 2012/ 20/70 / 20/40-

3 [00107] June 2013/ 20/60 / 20/30

4 [00108] Example 7: Nutrient treatment of subjects having lutein and zeaxanthin
5 deficiencies can improve retinal RNFL fibrosis.

6 [00109] Subject Description: Patient 1548 is a 54 year old male who had a history of
7 heavy drinking (40 ounces hard liquor daily) until 2009. Upon examination on July 26, 2010,
8 while the patient was taking lutein (5 mg) and zeaxanthin (0.25 mg daily), the patient had an
9 OD NDS of 3 (FIG. 4A) and an OS NDS of 5 (FIG. 4B) accompanied by severe OS retinal-
10 RNFL fibrosis (FIG. 4C). It is contemplated that the patient also had stenosis of the left
11 carotid artery, correlated with the severe fibrosis and poor NDS.

12 [00110] Treatment 1: Lutein (5 mg) daily and fish five times per week for over 24 months.

13 [00111] Results: Upon examination of November 13, 2012, the patient had an OU NDS of
14 4 (FIGS. 4D and E).

15 [00112] Treatment 2: LZO3P daily.

16 [00113] Results: Upon examination on June 4, 2013, the patient's fibrosis had resolved
17 and he had an OU NDS of 3 (FIGS. 4F and G), indicating that the patient's risk for chronic
18 disease had been reduced following LZO3P treatment.

19 [00114] Example 8. Nutrient treatment of subjects having lutein and zeaxanthin
20 deficiencies can improve wet AMD.

21 [00115] Wet AMD occurs when ischemic retinal tissue secretes vascular endothelial
22 growth factor (VEGF), which causes growth of fragile new blood vessels that leak fluid and
23 blood. This edema and hemorrhaging damages retinal tissue and reduces vision. Intra-
24 vitreal injection of anti-VegF compositions is the current standard of care for wet AMD.
25 However, it is contemplated that such injections do not treat the ischemia that is
26 contemplated to underlie wet AMD.

27 [00116] Subject Description: Patient 610 is a 70 year old male who was found to have an
28 OD NDS of 2-3 and dry AMD (FIG. 5A) and an OS NDS of 4-5 and wet AMD (FIG. 5B) upon

1 examination on June 4, 2009. The patient was referred to retinal specialist who did not
2 prescribe eye nutrient supplementation, but prescribed monthly intravitreal anti-VEGF
3 injections into his left eye. Upon examination on March 4, 2011, the patient had an OD NDS
4 of 3 and dry AMD (FIG. 5C) and an OS NDS of 5 (FIG. 5D), OS geographic atrophy and
5 ERM (FIG. 5E).

6 **[00117]** Treatment: One Vitalux plus omega™ pill twice daily (total daily dose of 5 mg
7 lutein, 1 mg zeaxanthin, 200 mg EPA and 100 mg DHA).

8 **[00118]** Results: Upon examination on November 6, 2012, the patient had an OD NDS of
9 5 and his OD dry AMD had worsened (FIG. 5F). However, the patient had an OS NDS of 3
10 (FIG. 5G), and the OS choroidal nonperfusion and GA were reversing and the OS ERM was
11 absent (FIG. 5H). It is contemplated that the failure of the OD improvement is associated
12 with carotid stenosis. It is contemplated that the failure of the OD improvement is associated
13 with carotid stenosis of the right CCA and/or ICA. This low dose of lutein and zeaxanthin is
14 not enough to prevent or reverse carotid artery stenosis.

15 **[00119]** Subject Description: Patient 2363 is a 93 year old female who had a history of
16 wet AMD and intravitreal injections in her OS. Upon examination on April 13, 2012, the
17 patient was taking 2 Vitalux Plus Omega™ pills twice daily with meals Total daily dose of
18 lutein, 10 mg, zeaxanthin, 2 mg, EPA 400 mg, DHA 200 mg, plus other antioxidants. Despite
19 this "standard of care" nutrient therapy, the patient was developing early wet AMD in her OD.
20 The patient's OS had macular scarring and GA and an OS NDS of 3 (FIG. 5I) and an OD with
21 wet AMD and an NDS of 5 (FIG. 5J). It is contemplated that the patient had a right carotid
22 stenosis. She was referred to a retinal specialist.

23 **[00120]** Upon examination on October 5, 2012, the patient had received an intravitreal
24 injection in her right eye in August 2012 (FIG. 5K).

25 **[00121]** Treatment: 2 Vitalux plus omega twice daily with meals and 20 mg lutein and 5
26 mg zeaxanthin with supper.

27 **[00122]** Results: Upon examination on February 5, 2013, the patient had an OD NDS of 5
28 (FIG. 5L) and her OD had macular microheme (FIG. 5M). The patient had an OS NDS of 3
29 (FIG. 5N).

30 **[00123]** Upon examination on April 30, 2013, the patient had an OD NDS of 3 (FIG. 5O)
31 and the OD macular microheme was absent (FIG. 5P). The patient had an OS NDS of 3

1 (FIG. 5Q). The patient's probable right carotid stenosis was resolving and it was
2 contemplated that full vascular perfusion OU should prevent recurrent wet AMD OU.

3 **[00124]** Unfortunately, miscommunication resulted in the patient reverting back to 2
4 Vitalux plus Omega™ pills, twice daily with meals. She was seen August, 2013 with an
5 episode of total black out of vision in her right eye for 24+ hours. Her OD NDS was again 5,
6 confirming a right carotid stenosis that caused her temporary right eye stroke.

7 **[00125]** Discussion: Results of the AREDS 2 study, released June 2013, indicate that 10
8 mg lutein, 2 mg zeaxanthin and antioxidants is not a combination that is adequate to treat
9 moderate to severe eye disease. This LZO3P study and the four year study of VRT patients
10 concur. (table 1 and table 2) It is contemplated that an advanced stage of carotid arterial
11 stenosis is present on the same side(s) of the head as moderate to severe eye disease.
12 Daily doses of at least 20 mg lutein and 5 mg of zeaxanthin are required to treat advanced
13 carotid arterial sclerosis.

14 **[00126]** Measuring the lutein and zeaxanthin pigment density for the entire posterior pole
15 of the eye, using the methods disclosed herein provides a complete geographic
16 measurement that demonstrates the areas of the eye that are deficient in lutein and the
17 areas of the eye that are deficient in zeaxanthin. Lutein deficiency is seldom the same level
18 as zeaxanthin deficiency. It is contemplated that lutein and zeaxanthin levels reflect: i) the
19 level of blood supply to each eye; ii) the level of absorption of lutein and zeaxanthin from the
20 intestine; and iii) the level of consumption of lutein and zeaxanthin rich foods or
21 supplements.

22 **[00127]** Example 9. Nutrient treatment of subjects having lutein and zeaxanthin
23 deficiencies can improve vitreoretinal traction disorders.

24 **[00128]** Subject Description: Patient 730, a 74 year old male, upon examination in
25 November 2010, the patient had an OD NDS of 3 (FIG. 6A) and an OS NDS of 4 (FIG. 6B).
26 The patient had an OD central macular edema (CME) (FIG. 6C) and an OS macular pucker
27 (FIG. 6D).

28 **[00129]** Treatment: Lutein (10 mg) and zeaxanthin (2 mg) daily.

29 **[00130]** Results: Upon examination in November 2011, the patient had an OD NDS of 2
30 (FIG. 6E and G) and an OS NDS of 2 (FIG. 6F and H) and macular pucker had improved.

- 1 [00131] Treatment: Lutein (20 mg) and zeaxanthin (5 mg) daily.
- 2 [00132] Results: Upon examination in May 2012, following 6 months of treatment,
3 reversal of CME (FIG. 6I and K) and macular pucker (FIG. 6J and L) were evident and the
4 patient had an OU NDS of 2.
- 5 [00133] Subject Description: Patient 402 is a 54 year old female who, upon initial
6 examination in April 2009, the patient had an OD NDS of 4 (FIG. 6M) and an OS NDS of 4
7 (FIG. 6N). The patient had an OS ERM (FIG. 6 O).
- 8 [00134] Treatment: Lutein (20 mg) and zeaxanthin (5 mg) daily.
- 9 [00135] Results: Upon examination in November 2010, the patient had an OU NDS of 3
10 (FIGS. 6P and Q). The patient's OS ERM was reversed (FIG. 6R).
- 11 [00136] Treatment 2: Lutein (20 mg) and zeaxanthin (5 mg) daily.
- 12 [00137] Results: Upon examination in March 2012, the patient had an OD NDS of 4 (FIG.
13 6S) and an OS NDS of 3 (FIG. 6T). The OD NDS demonstrated reduced perfusion in the
14 vascular arcades of the right eye. It is contemplated that this is due to early right carotid
15 stenosis. It is contemplated that this may increase the patient's risk of right CRVO or BRVO.
- 16 [00138] Example 10. LZO3P treatment of subjects having lutein and zeaxanthin
17 deficiencies can prevent BRVO.
- 18 [00139] Subject Description: Patient 759 is a 75 year old male. He became diabetic in
19 1994. Eye exams between 2001 and 2007 were normal and the patient's VA was 20/20 in
20 each eye. In 2008, his right eye had developed mild diabetic retinopathy and VA decreased
21 to 20/30 in each eye. June 2009, he had heart bypass surgery. Upon examination on August
22 2009, he had mild diabetic retinopathy in both eyes and NDS was 3.5 OU (FIGs 7A and B).
- 23 [00140] Upon examination on August 10, 2010, the patient had early OD CRVO (FIG.
24 7C). NDS cannot be measured in acute BRVO; therefore, OD NDS is not reported. The
25 patient's OS had an NDS of 4 (FIG. 7D). Patient's VA was 20/25 in each eye.
- 26 [00141] The patient received Lucentis intravitreal injections monthly from August 2010
27 through August 2011 and injections every 6 weeks thereafter. Upon examination on
28 September 8, 2011, the patient's OD had a VA of 20/400 (only scanning vision) (FIG. 7E)
29 and an OS of 20/40 (FIG. 7F). The retinal arteries of the posterior pole were almost

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1 completely blocked. The right eye had end-stage microvascular non-perfusion of the
2 posterior pole retina. His left eye arteries remained perfused and usable vision remained of
3 20/40.

4 **[00142]** Upon examination of March 8, 2012, the patient's OD had a VA of 20/400 with
5 central scotoma (FIG. 7G) and an OS VA of 20/40 (FIG. 7H).

6 **[00143]** Injections continued to Sept. 2012, at which time OD VA was CF at 10 feet. (CF
7 = count fingers). The inferior artery was now a white ghost vessel. Patient was prescribed
8 LZO3P. Injections continued and patient developed severe pain and redness (presumed
9 endophthalmitis).

10 **[00144]** May 2013 exam, OD massive hemorrhaging was present (FIG. 7F). OS VA was
11 mildly improved to 20/30+.

12 **[00145]** Subject Description: Patient 272 is a 47 year old male who was examined on
13 March 09, 2009 and May 10, 2012. At both of those visits VA was 20/20 in each eye and
14 NDS was 3.5 in each eye (FIG. 8A).

15 **[00146]** Upon examination on March 25, 2013, patient had a left branch retinal vein
16 occlusion and BRVO that was likely at least 6 months old. He had an OU NDS of 3.5 and a
17 visual acuity of OD 20/20 and OS 20/200. OD VA remained 20/20 throughout the following
18 treatment period.

19 **[00147]** Treatment: LZO3P daily.

20 **[00148]** Results: Upon examination of April 26, 2013, the patient had an OU NDS of 3
21 (FIG. 8B) and an OS VA of 20/80. Swelling and hemorrhages were reduced and
22 arteriovenous crossings were normalizing. Following this examination the patient began
23 taking Lipitor in addition to LZO3P.

24 **[00149]** Upon examination on May 28, 2013, the patient's OS VA was 20/40. However,
25 the patient's OU NDS was 3.5 (FIG. 8C). Following treatment, the patient's chorioidal
26 swelling decreased and retinal swelling decreased (FIGS 8D-F; choroid in upper right
27 quadrant, retina in bottom left quadrant).

28 **[00150]** Upon examination July 17, 2013, the patient's OS VA remained 20/40. However,
29 the patient's OU NDS remained 3.5. It is contemplated that something interfered with

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1 nutrient absorption and/or nutrient delivery to the patient's eyes. Despite the continued NDS
2 of 3.5, the patient's choroidal swelling and retinal swelling decreased further.

3 **[00151]** Example 11. LZO3P treatment of subjects having lutein and zeaxanthin
4 deficiencies can prevent retinal detachment.

5 **[00152]** Subject Description: Patient 182 is a 63 year old male who was experiencing
6 flashing lights in his vision. On May 15, 2013, examination revealed a horseshoe-shaped
7 chorioretinal geographic atrophy in the inferior nasal peripheral retina (FIG. 9A and B). The
8 patient had an OD NDS of 4 (FIG. 9C) and an OS NDS of 3 (FIG. 9D). It is contemplated
9 that the patient had OD MVNP, secondary to choroidal non-perfusion, partial retinal arterial
10 arcade non-perfusion, or secondary to right carotid stenosis, (internal and/or common
11 carotid) causing reduced perfusion on the right side. The patient's posterior pole was
12 unremarkable.

13 **[00153]** Patient was prescribed LZO3P and was reexamined in August 2013. NDS of the
14 peripheral retina improved from 4 to 3. Choroidal perfusion was improved. The smaller
15 portion of the "horse shoe" seemed to be less atrophic. Posterior pole NDS became worse.
16 It is contemplated that central retinal artery non-perfusion requires longer therapy of 6 to 12
17 months duration, to show improvement.

18 **[00154]** Example 12. Treatment of subjects having lutein and zeaxanthin deficiencies can
19 reverse retinal arteriole sclerosis.

20 **[00155]** Subject Description: patient 531 is a 66 year old female. Upon initial examination
21 on October 4, 2012, the patient had an OU NDS of 5 (FIGS. 10A and B). Her central retinal
22 arteries were one half occluded.

23 **[00156]** Treatment: LZO3P daily.

24 **[00157]** Results: Upon examination on May 2, 2013, the patient had an OU NDS of 2
25 (FIGS. 10C and D) and her arteries were fully perfused.

26 **[00158]** Example 13. LZO3P treatment of subjects having lutein and zeaxanthin
27 deficiencies can reverse presumed choroidal sclerosis.

28 **[00159]** Subject Description: Patient 252 is an 86 year old female. Upon initial
29 examination on November 19, 2012, the patient had an OU NDS of 5 (FIGS. 11A and B).
30 The patient exhibited non-perfusion, retina-RNFL fibrosis, excavation and VA LP OU.

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- 1 [00160] Treatment: LZO3P daily.
- 2 [00161] Results: Upon examination on March 18, 2013, the patient had an OU NDS of 3
3 (FIGS. 11C and D). The patient's choroidal blood vessels had increased in diameter,
4 indicating reperfusion. Retina-RNFL fibrosis had reversed and excavation was reduced. No
5 improvement of VA was apparent.
- 6 [00162] Example 14. Statin or LZO3P treatment of subjects having lutein and zeaxanthin
7 deficiencies can reverse presumed unilateral carotid stenosis.
- 8 [00163] Subject Description: Patient 0237 is a 63 year old female. Upon initial
9 examination on November 13, 2012, the patient had an OD NDS of 3 and an OS NDS of 5.
10 The patient had a left retinal hemorrhage and was referred to a general practitioner for
11 carotid assessment, wherein the patient was found to have a left carotid artery stenosis. The
12 patient's general practitioner prescribed doubled dosage of the cholesterol medication that
13 the patient was taking.
- 14 [00164] Upon examination on February 19, 2013, the patient's OD NDS had improved to
15 2 and OS NDS had improved to 3. Further, the patient's left retinal hemorrhage had
16 resolved. The statin medication the patient was taking appears to have resolved the
17 presumed unilateral carotid stenosis and unilateral eye disease.
- 18 [00165] Patient 0895 is a 71 year old male. Upon initial examination on September 27,
19 2010, the patient had mild OS ERM. OD NDS was 2, OS NDS was 4. Left partial carotid
20 stenosis was presumed.
- 21 [00166] Treatment: Lutein (10mg) and zeaxanthin (2mg) daily.
- 22 [00167] Results: Upon examination on October 4, 2011, the patient had an OD NDS of 1
23 and an OS NDS of 4. The mild OS ERM increased slightly. Twelve months on Lutein (10mg)
24 and zeaxanthin (2mg) daily did not result in increased blood flow to the left eye.
- 25 [00168] Treatment: Lutein (20mg) and zeaxanthin (5mg) daily.
- 26 [00169] Upon examination on April 16, 2012, the patient had an OD NDS of 2 and an OS
27 NDS of 2. The patient's ocular nutrient health had improved and equalized and the patient's
28 OS ERM had resolved. Lutein (20mg) and zeaxanthin (5mg) daily did result in increased
29 blood flow to the left eye. It is contemplated that lutein (20mg) and zeaxanthin (5mg) daily
30 can reverse partial carotid artery stenosis.

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1 **[00170]** Example 15: Subject who declined nutrient therapy.

2 **[00171]** Subject Description: Patient 1423 is a 65 year old male. Upon initial examination
3 on May 20, 2010, the patient exhibited an OU NDS 2, OU normal (FIG. 12A).

4 **[00172]** Upon examination on May 28, 2012, the patient had an OD NDS of 4 and an OS
5 NDS of 3.5. The patient's OD had an ERM involving most of the posterior pole between the
6 vascular arcades (FIG. 12B) and retinal puckering temporal to the optic nerve head. The
7 patient declined nutrient therapy.

8 **[00173]** Upon examination on November 29, 2012, the patient had an OD NDS of 4 and
9 an OS NDS of 3.5. The patient's OD exhibited a large ERM with increasing fibrosis (FIG.
10 12C). The patient declined nutrient therapy.

11 **[00174]** Upon examination on May 30, 2013, the patient had an OD NDS of 4 and an OS
12 NDS of 3. The patient's OD ERM remained large (FIG. 12D). The patient declined nutrient
13 therapy.

14 **[00175]** Example 16: Perfusion level of various vascular supplies

15 **[00176]** It has been found that the pattern of light and dark in the retinal fibre layer can be
16 analyzed in relation to the perfusion level in the macula, the superior central retinal artery,
17 the inferior central retinal artery, the choriocapillaris (choroid) and the optic nerve head.

18 **[00177]** The results shown in table 3 demonstrate the perfusion level of various vascular
19 supplies that occur in eyes at risk of eye disease and eyes with ocular diseases. These
20 perfusion levels increase with nutrient supplementation as described elsewhere in this
21 application. (Lower numeric values correspond with improved perfusion secondary to
22 decreasing nutritional deficiency of lutein and zeaxanthin.)

23 **[00178]** In the table the patient's gender is indicated as 1 for female and 2 for male. The
24 term "prevention" is used to indicate intervention when NDS of 4 or 5 is present in any
25 vascular area. The term lens vacuole is used to indicate earliest sign of non-perfusion of
26 interocular lens and occurs in eye with some scores of 4. In the cases described in table 3
27 the term VMT vitreomacular traction is epiretinal membranes.

1 [00179] Table 3

Subject No.	Reason for Intervention Prevention	F = 1 M = 2	Birth Year	Exam Date	Right Eye Macula	sup CRA	Inf CRA	Choroid	ONH	Left Eye Macula	sup CRA	Inf CRA	Choroid	ONH
1		2	1939	1 11 13	4	5	5	4	4	3	4	4	3	4
				1 13 14	2	3	4	3	2	2	3	3	3	2
2		1	1938	1 11 13	3	5	5	3	4	3	5	5	3	4
				1 13 14	2	4	4	3	2	2	3	3	3	2
3		1	1971	5 23 13	4	3.5	3.5	4	3	4	3.5	3.5	4	3
				5 26 14	3	2	2	3	2	3	2	2	3	2
4	lens vacuole	1	1966	5 15 13	5	3.5	3.5	5	3	3.2	4	4	4	3
				11 14 13	4	3.2	3.2	4	3	3	3.2	3.2	3.5	3
5	left eye VMT	1	1966	4 11 14	2	3.5	3.5	3	2	2	4	4	4	2
6	right eye	2	1952	5 8 13	3	3.2	3.7	4	3	3	3.7	3.5	4	3
				11 22 13	3	3.5	3.5	3.5	3	3	3.5	3.5	3.5	3
				5 12 14	2	3	3	3	2	2	3	3	3	2
7	left eye	1	1946	11 26 13	4	4	5	4	3	4	4	5	4	3
				6 24 14	3	3	3	3.5	2	3	3	4	3	2
8	Dry AMD drusen both eyes	2	1944	3 25 13	5	3	3	4	4	5	3	3	4	4
				3 27 14	4	2	2	2	1	4	2	2	2	2
9	Dry AMD RPE left eye	1	1952	6 4 13	3	4	4	4	3	2	3.5	3.5	4	3
				9 8 14	2	3	3.5	3	2	1	3.2	3.2	3	2
10	Dry AMD	2	1945	5 23 13	4	4	4	5	4	4	3	3	3	3

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Subject No.	Reason for Intervention Prevention	F = 1 M = 2	Birth Year	Exam Date	Right Eye Macula	sup CRA	Inf CRA	Choroid	ONH	Left Eye Macula	sup CRA	Inf CRA	Choroid	ONH
	GA right eye													
				11 25 13	3	3	4	4	3	3	3	4	4	4
				5 26 14	3	3	4	3	3	3	2	3	2	2

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1 **[00180]** Although the invention has been described with reference to certain specific
2 embodiments, various modifications thereof will be apparent to those skilled in the art
3 without departing from the purpose and scope of the invention as outlined in the claims
4 appended hereto. Any examples provided herein are included solely for the purpose of
5 illustrating the invention and are not intended to limit the invention in any way. Any drawings
6 provided herein are solely for the purpose of illustrating various aspects of the invention and
7 are not intended to be drawn to scale or to limit the invention in any way. The disclosures of
8 all prior art recited herein are incorporated herein by reference in their entirety.

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WE CLAIM:

1. A method for identifying a subject having a nutritional deficiency, the method comprising:
 - a) obtaining an image of the subject's ocular posterior pole;
 - b) comparing the image to at least one reference ocular posterior pole image;
 - c) identifying a nutritional deficiency in the subject based on the comparison to the reference image,
 - wherein if the reference image is a healthy posterior pole, then an obtained image that comprises at least one region of increased contrast and/or decreased brightness relative to the reference image is indicative of the nutrient deficiency,
 - wherein if the reference image is a nutrient deficient posterior pole, then an obtained image that comprises at least one region of equal or increased contrast and/or equal or decreased brightness relative to the reference image is indicative of the nutrient deficiency, and
 - wherein the nutrient deficiency comprises a deficiency of one or more of lutein and zeaxanthin.
2. The method of claim 1, further comprising monitoring a subject for nutritional deficiency, wherein a subsequent image is obtained from the subject's posterior pole, compared with the image obtained in step a),
 - wherein if the subsequent image depicts increased contrast and/or decreased brightness relative to the image obtained in step a), then the subsequent image is indicative of lower nutrient levels in the subject's posterior pole, and
 - wherein if the subsequent image depicts decreased contrast and/or increased brightness relative to the image obtained in step a), then the subsequent image is indicative of higher nutrient levels in the subject's posterior pole.
3. The method of claim 1, further comprising assigning a score to the obtained image, wherein the score is based on a comparison between the obtained image and a reference database comprising posterior pole images obtained from a range of healthy and nutrient deficient subjects, wherein scores at opposite ends of the range are indicative of very healthy and severely nutrient deficient subjects, respectively.

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4. The method of claim 3, wherein the assigned score is indicative of lutein and zeaxanthin levels in the subject's posterior pole.

5. The method of claim 3 wherein the assigned score is indicative of microvascular perfusion levels in the subject's posterior pole.

6. The method of claim 1 wherein in step a) the image is obtained is a color retinal photograph and wherein the photograph is converted to grayscale images of the choroid, the retina and the retinal nerve fiber layer (RNFL).

7. The method of claim 6 wherein in the RNFL grayscale image is compared to a reference RNFL grayscale image in step b).

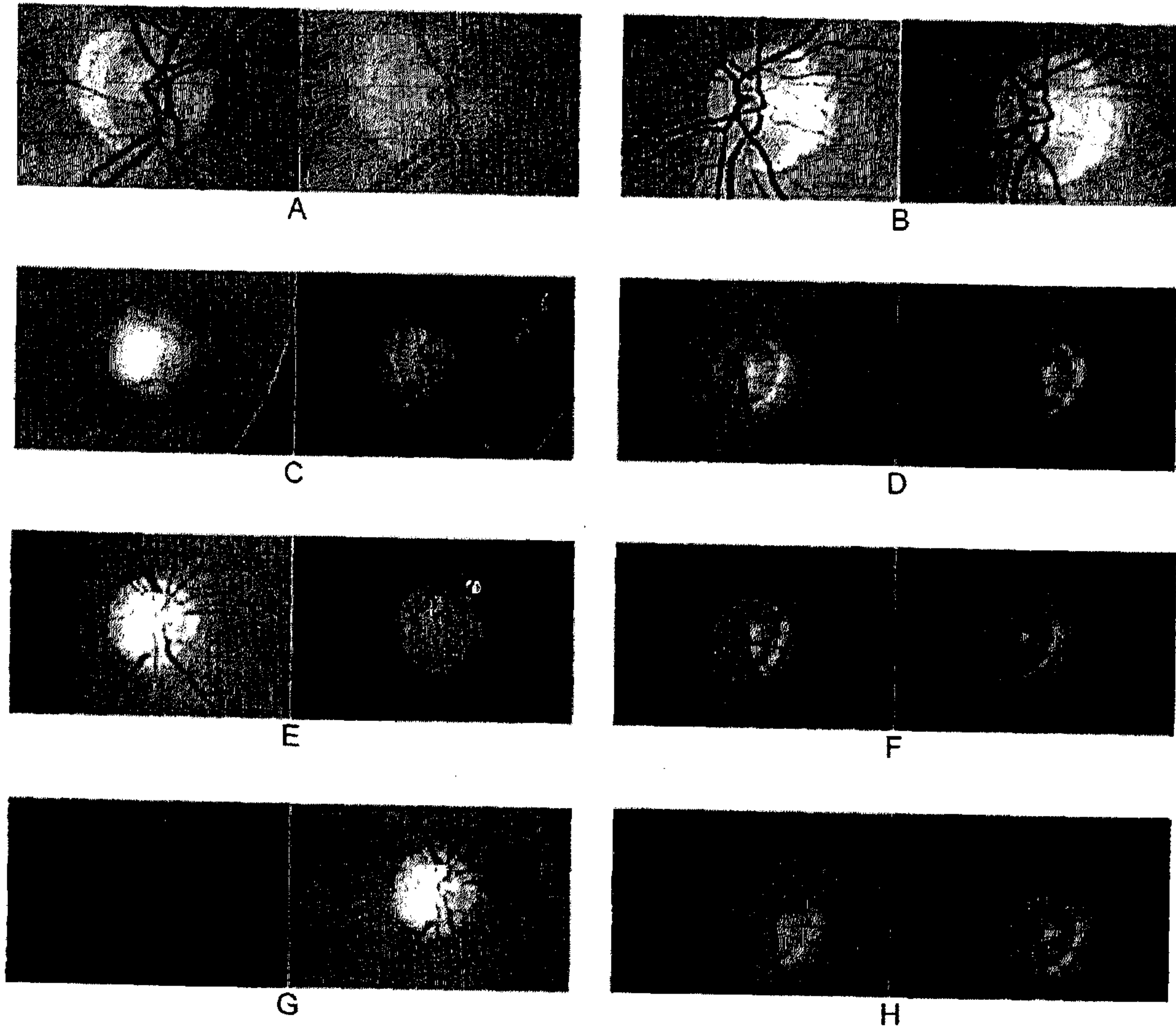


FIG. 1

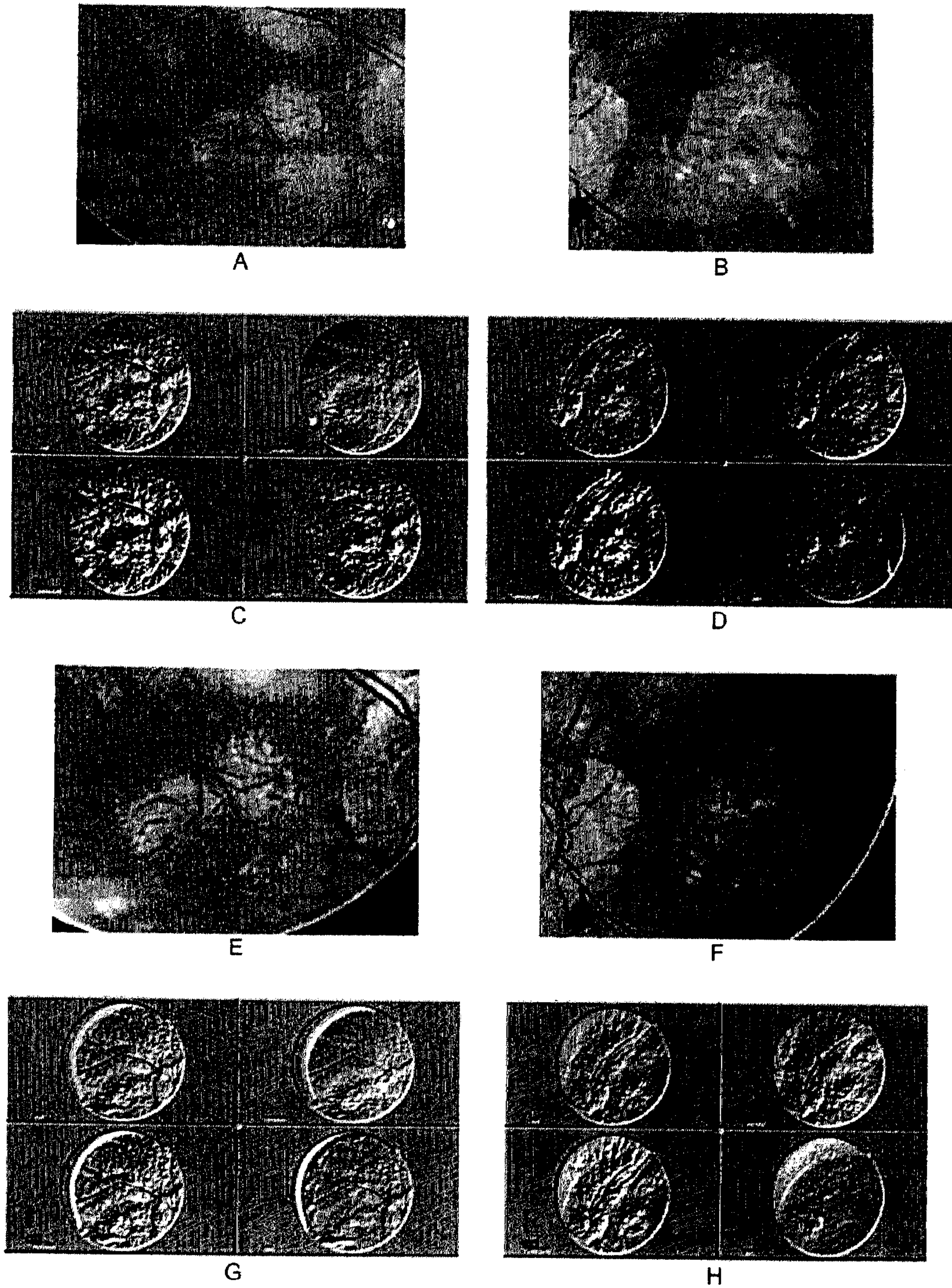
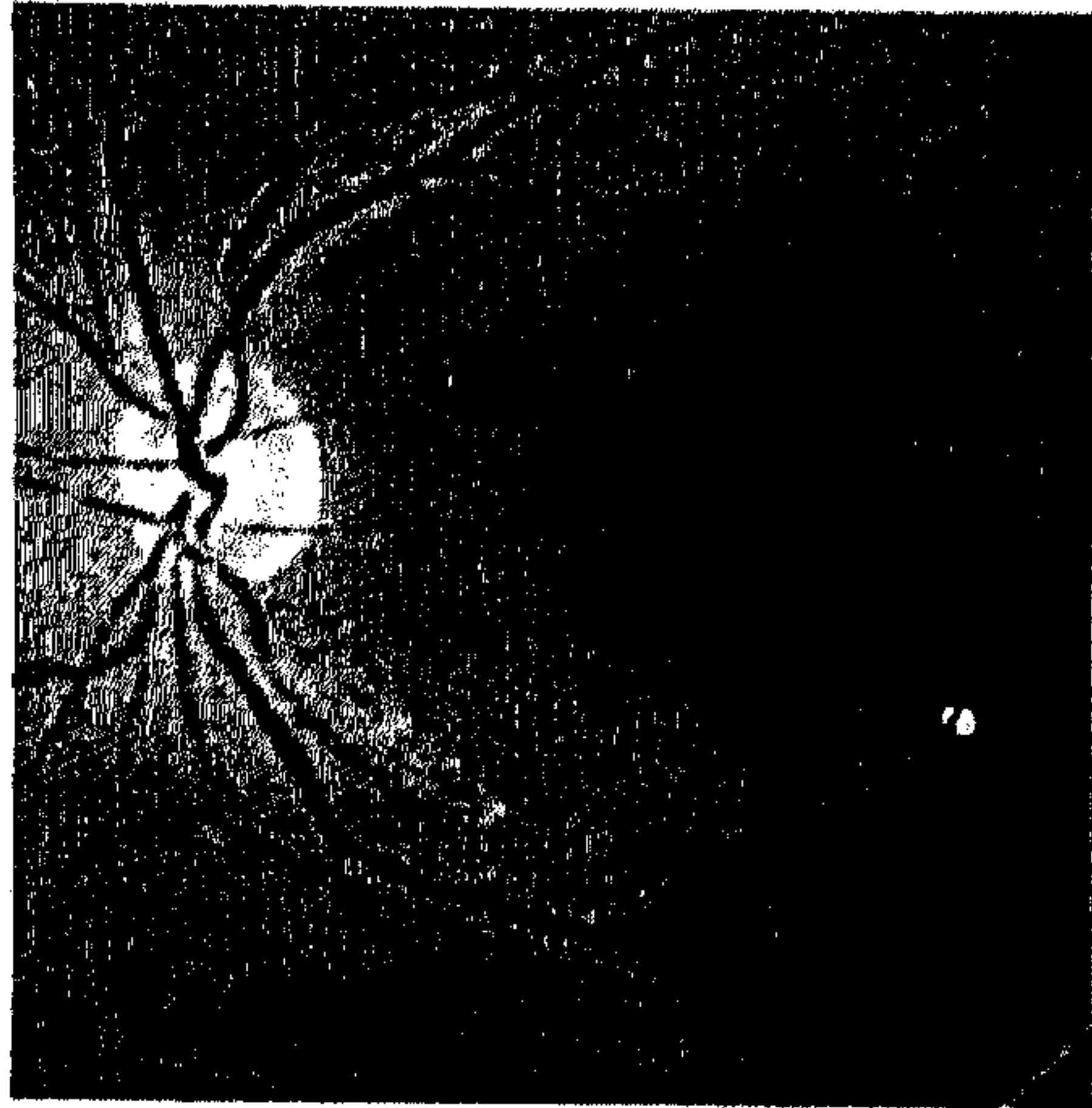
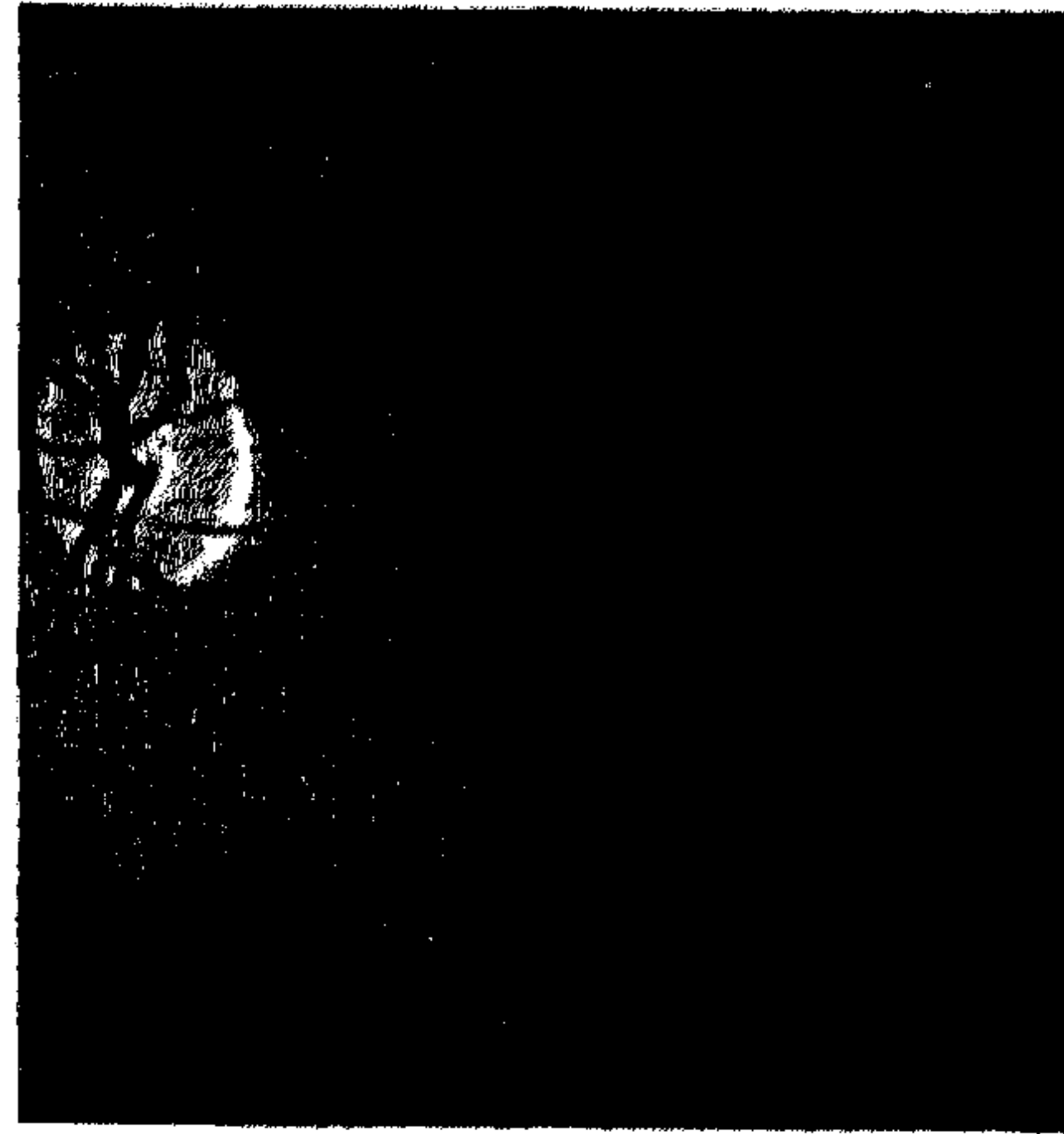


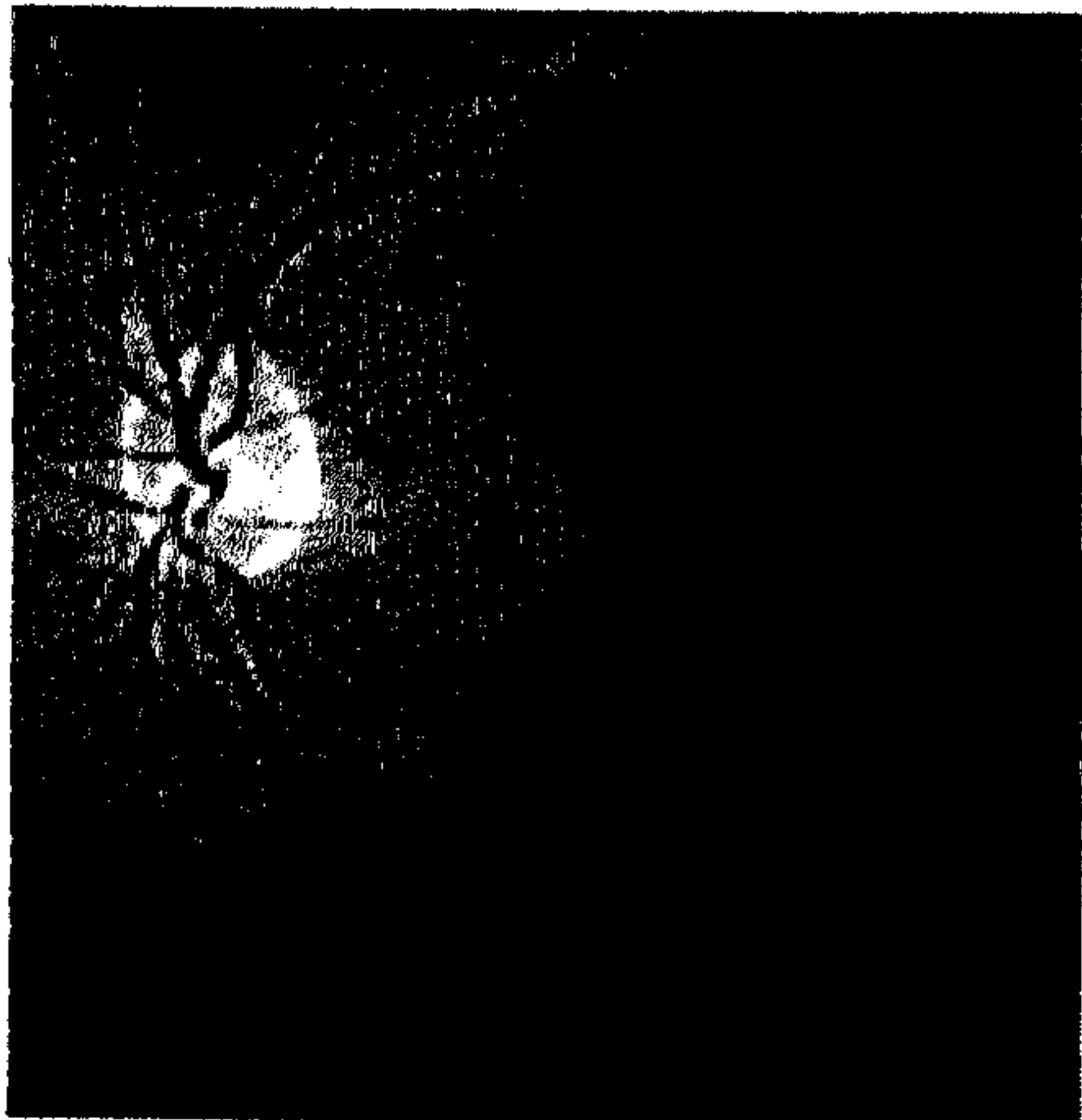
FIG. 2



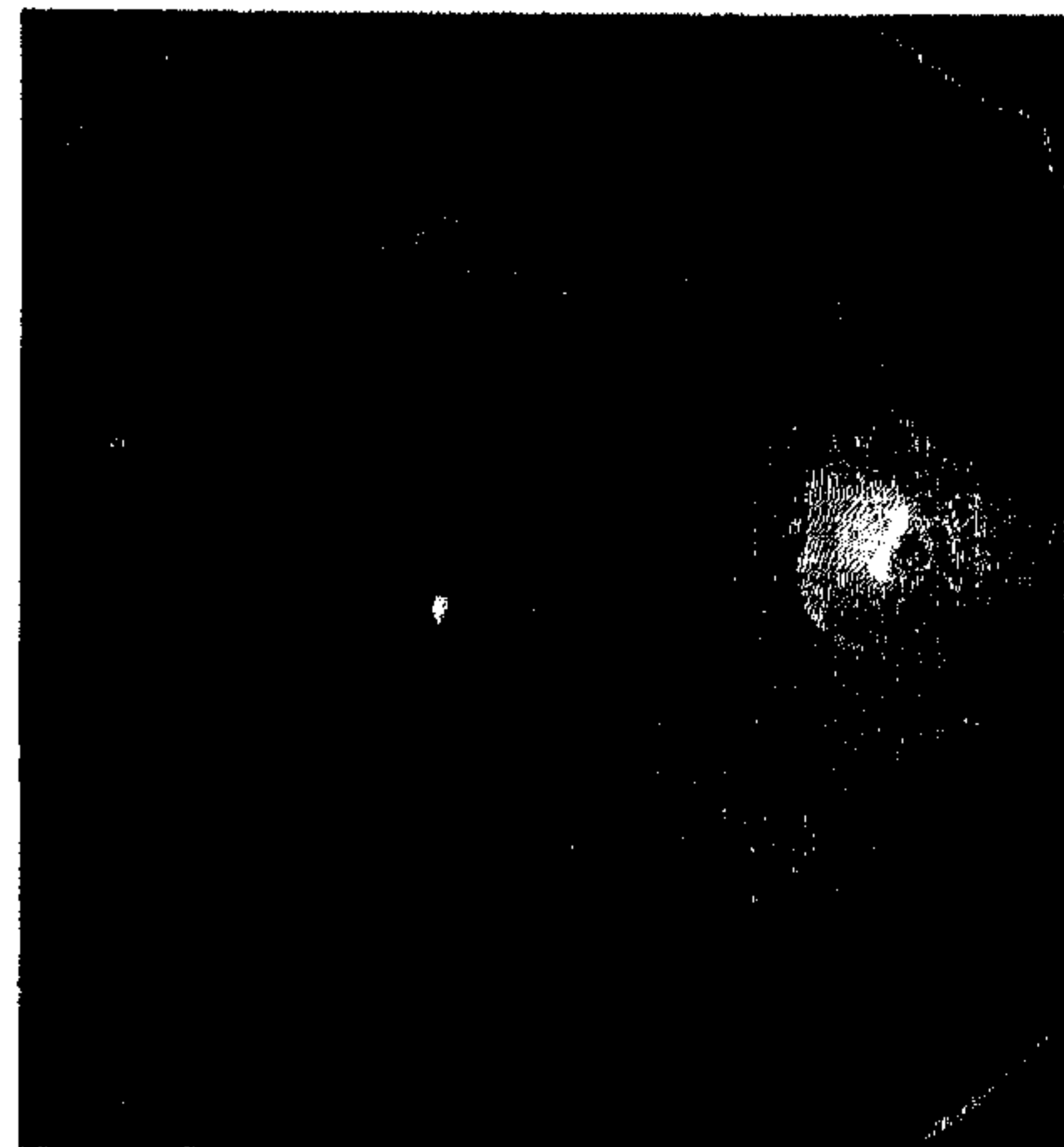
A



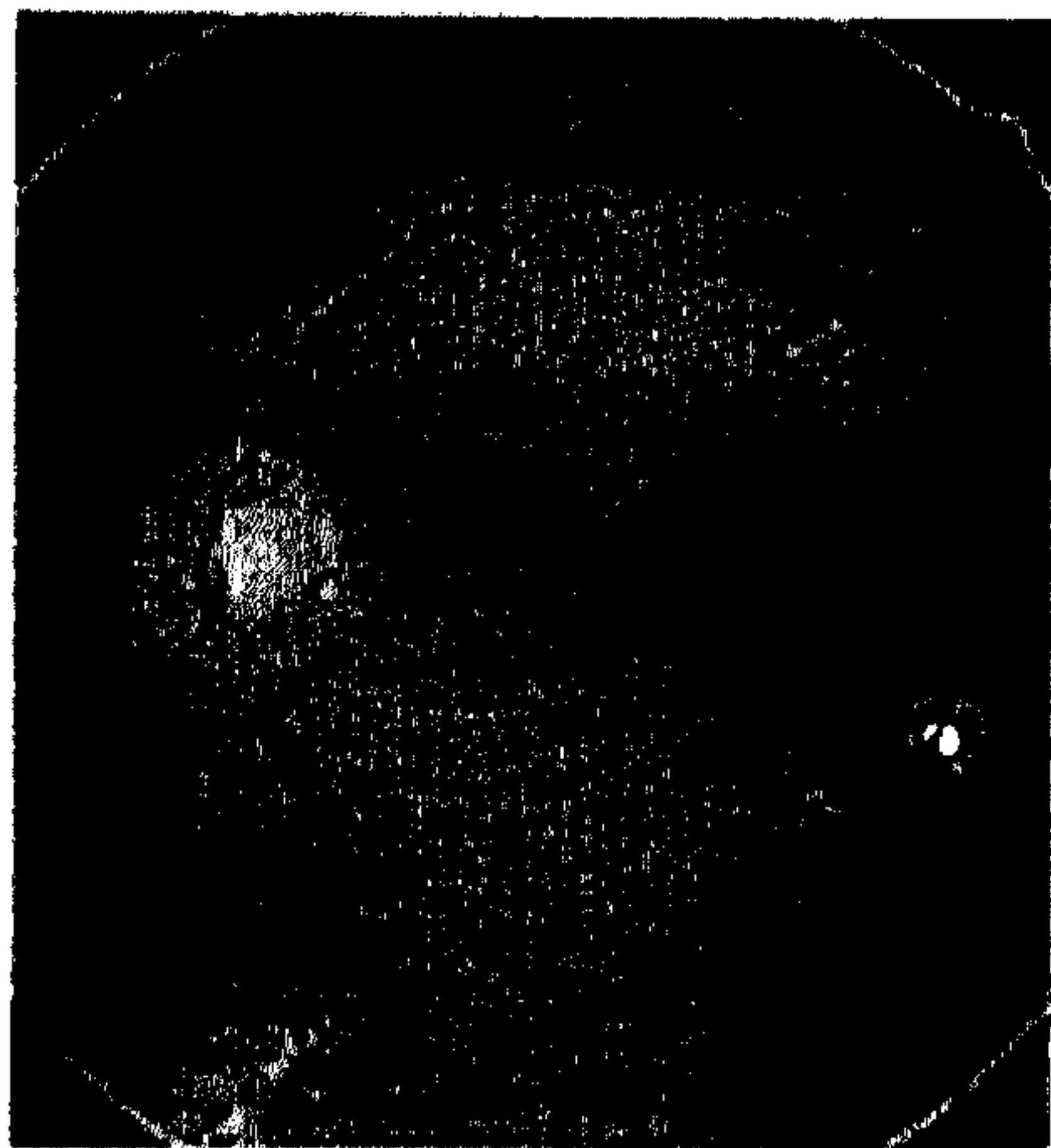
B



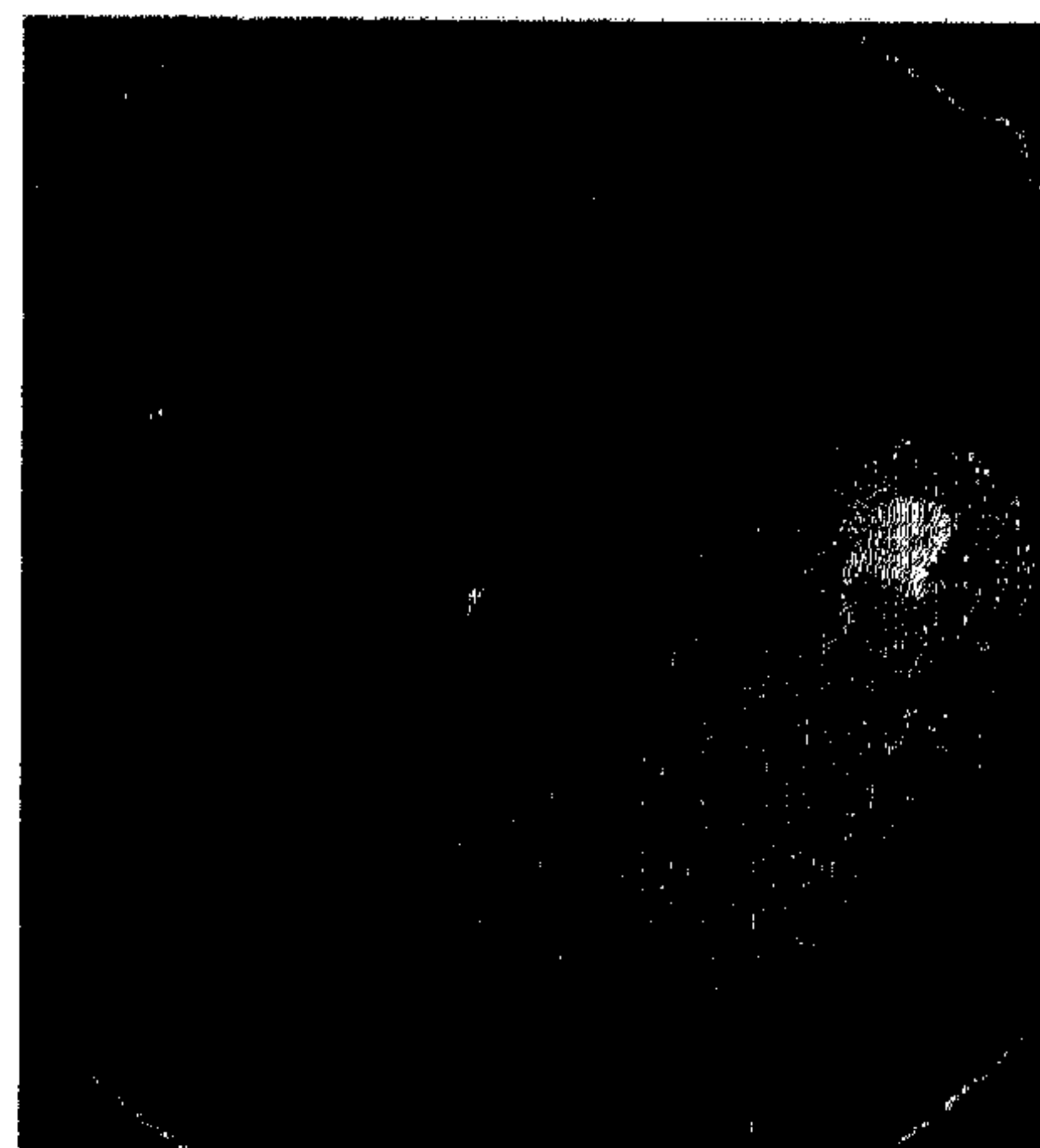
C



D

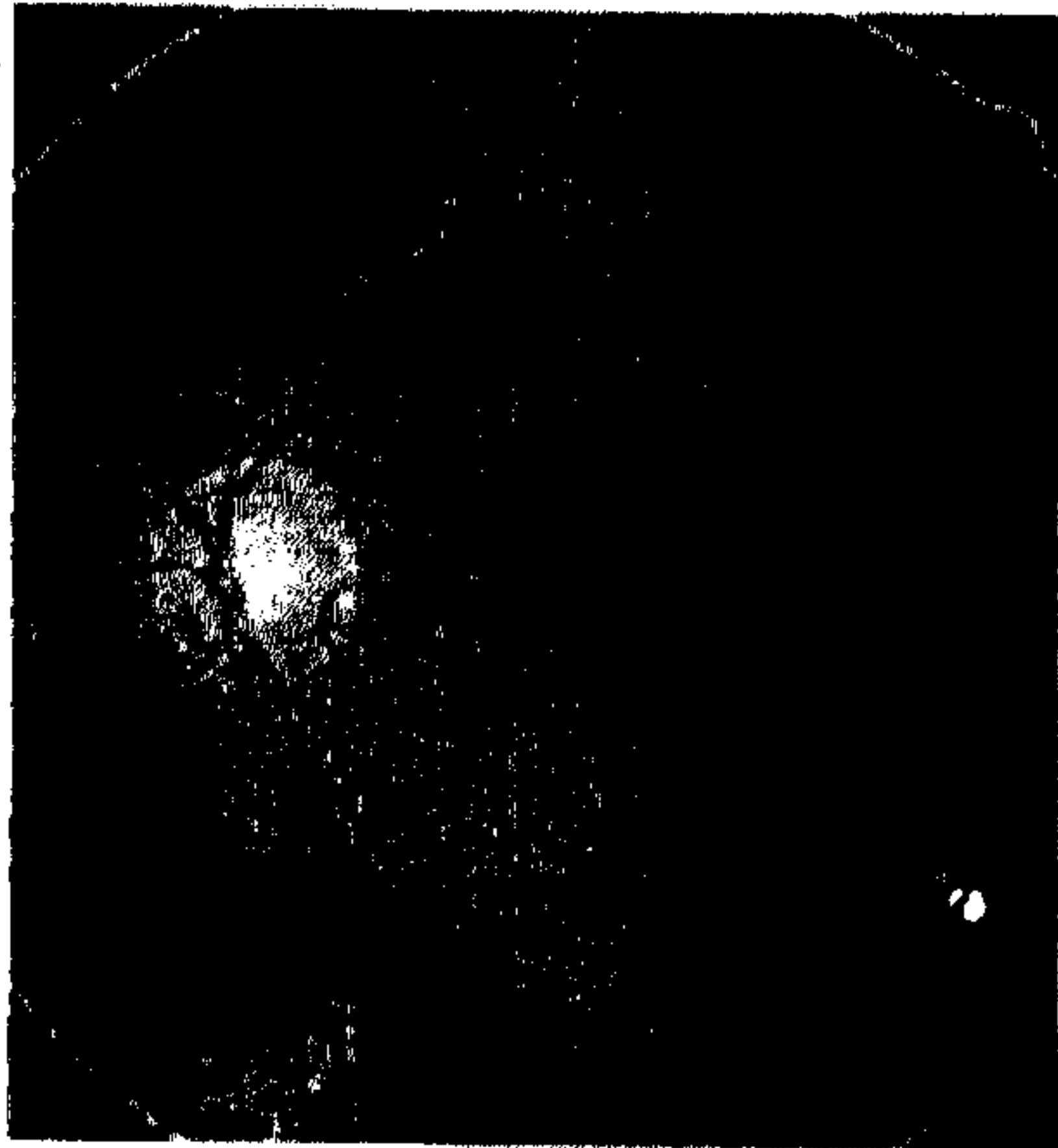


E

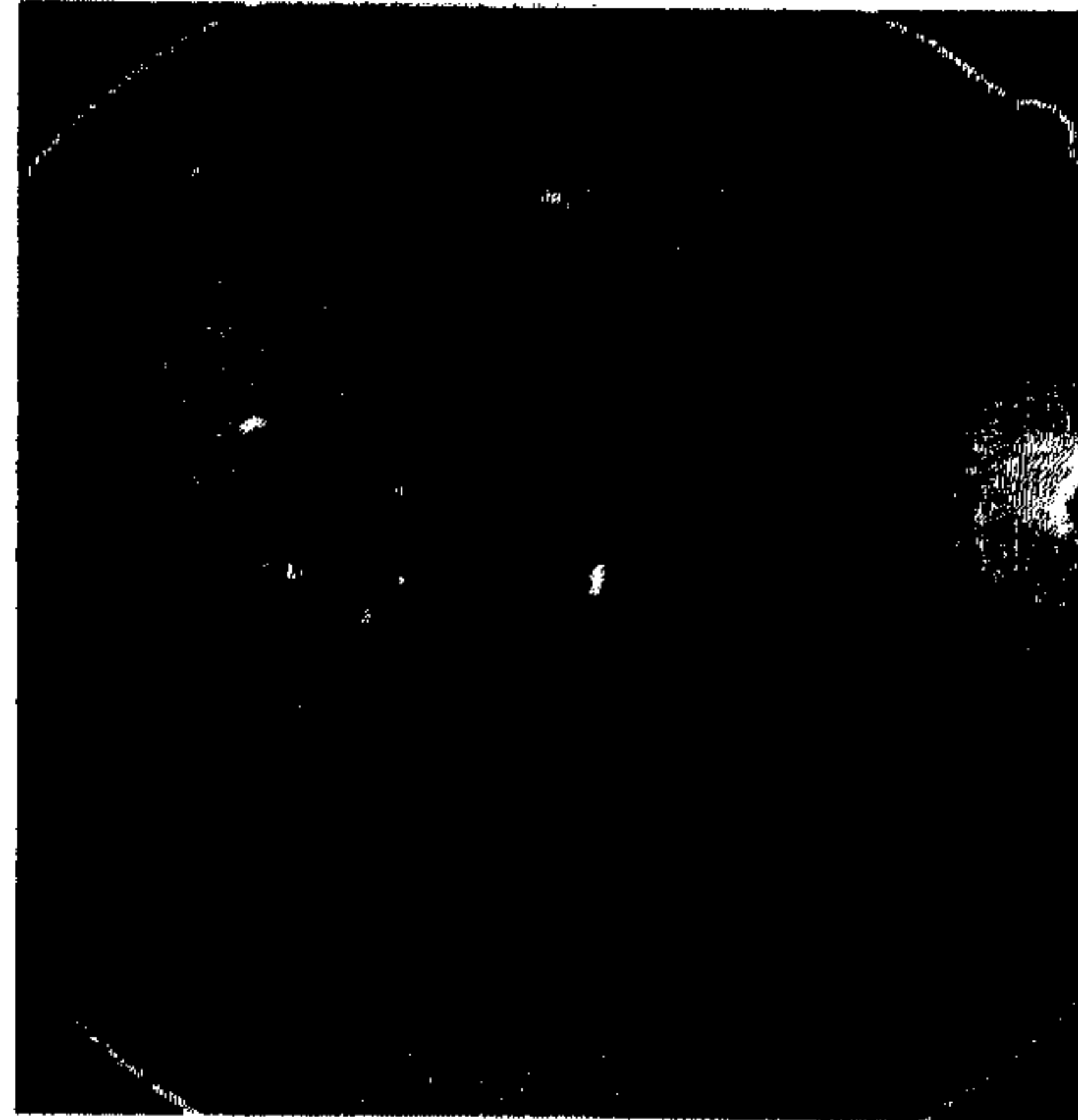


F

FIG. 3



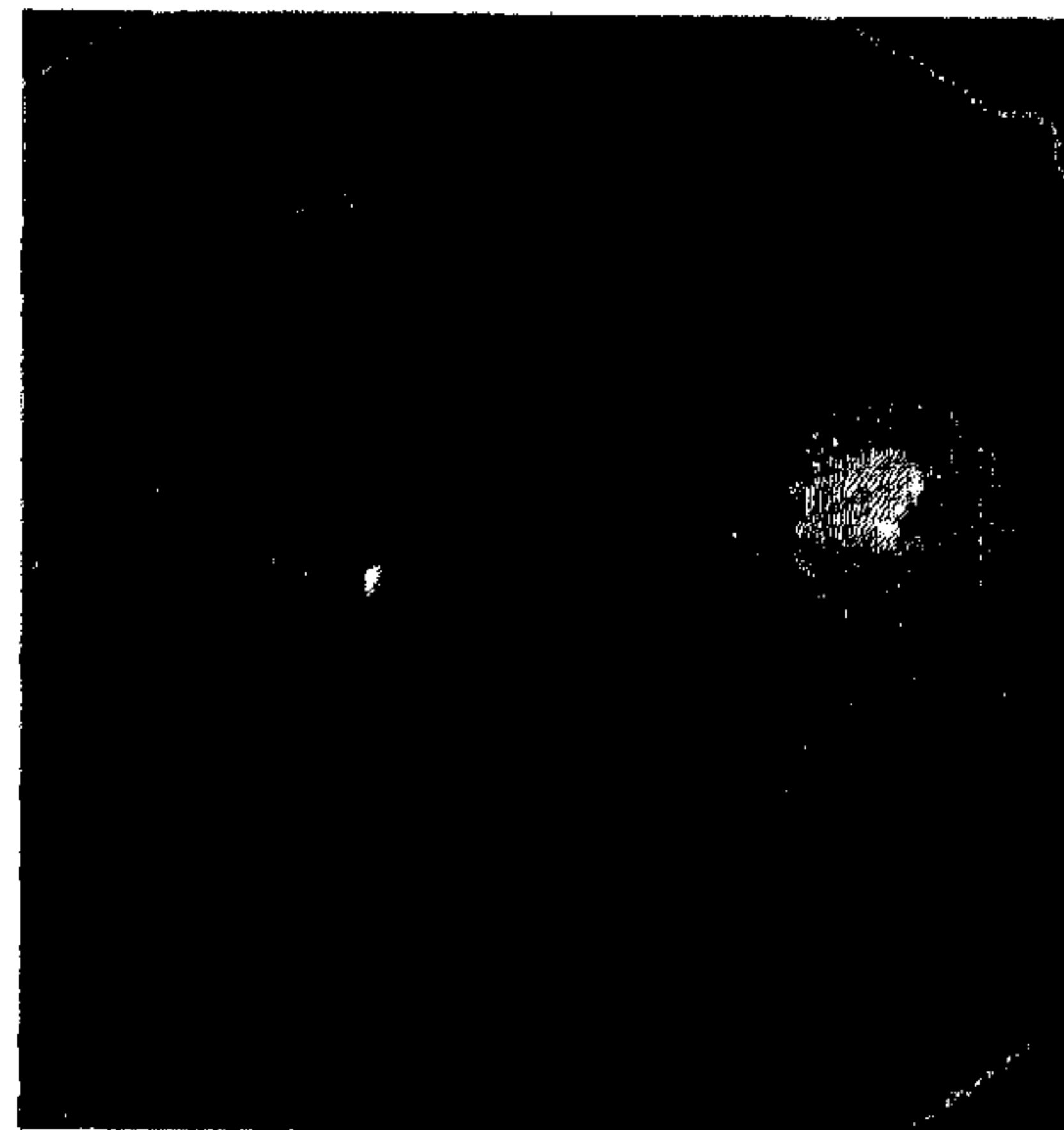
G



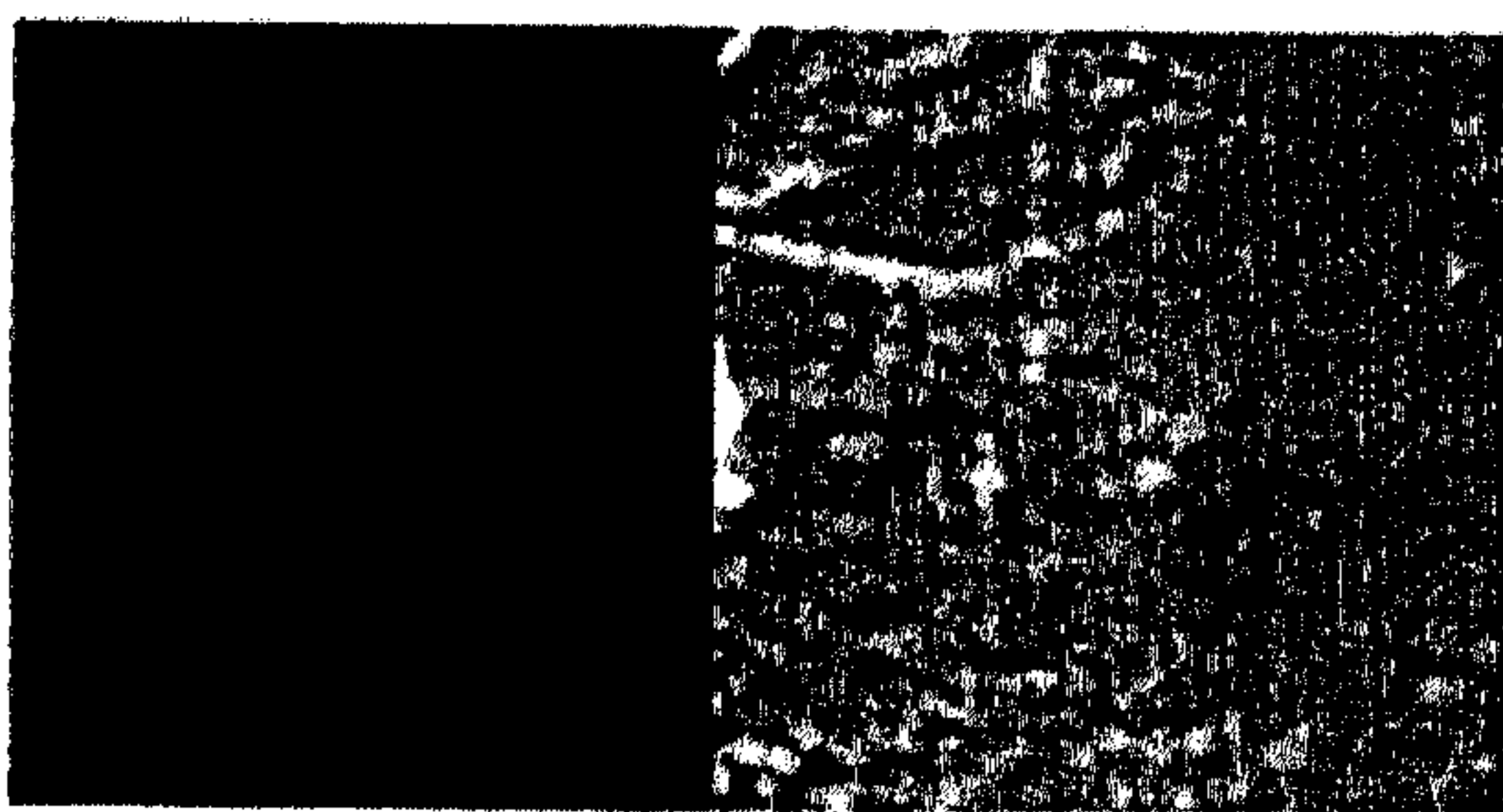
H



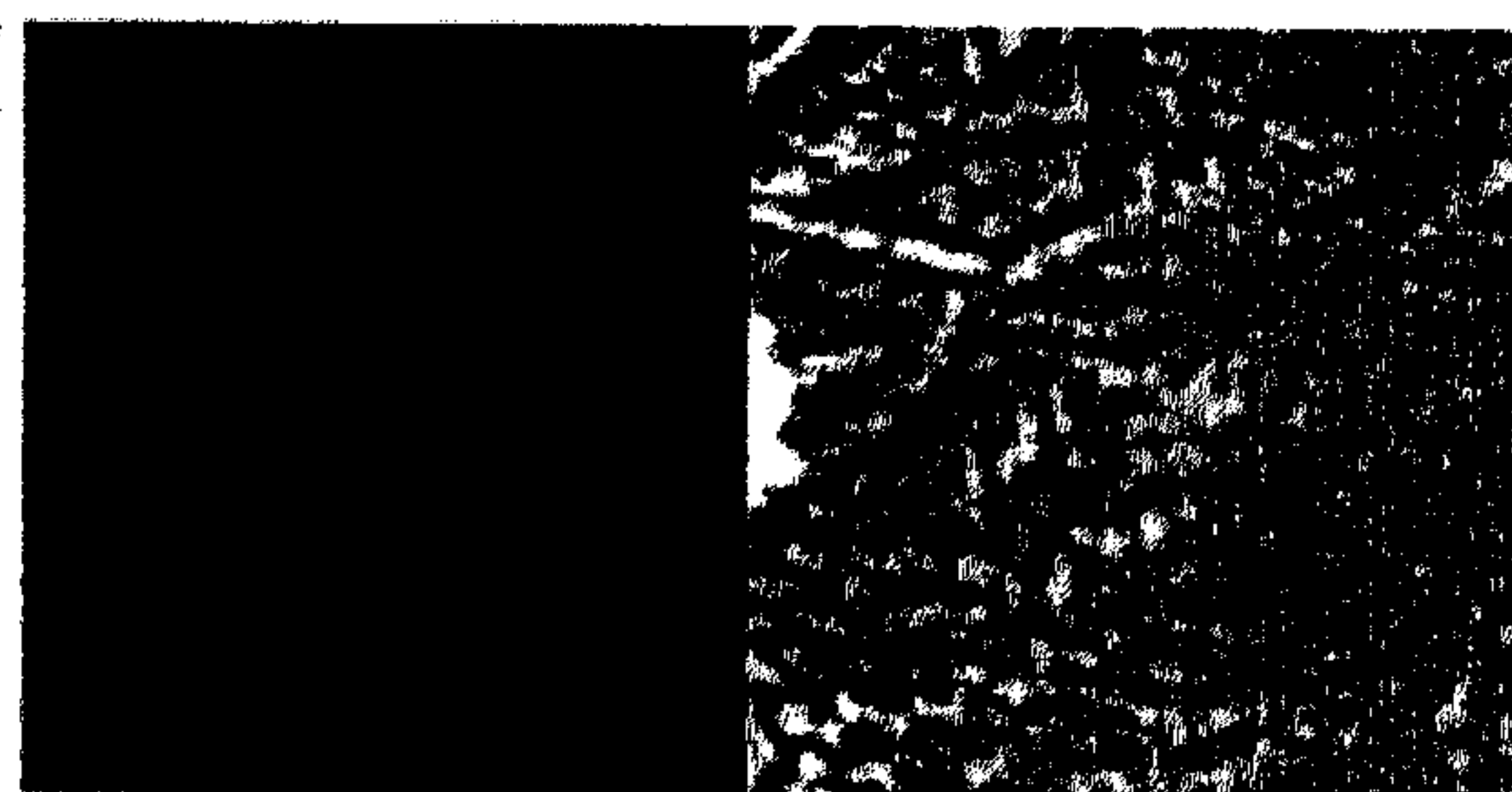
I



J

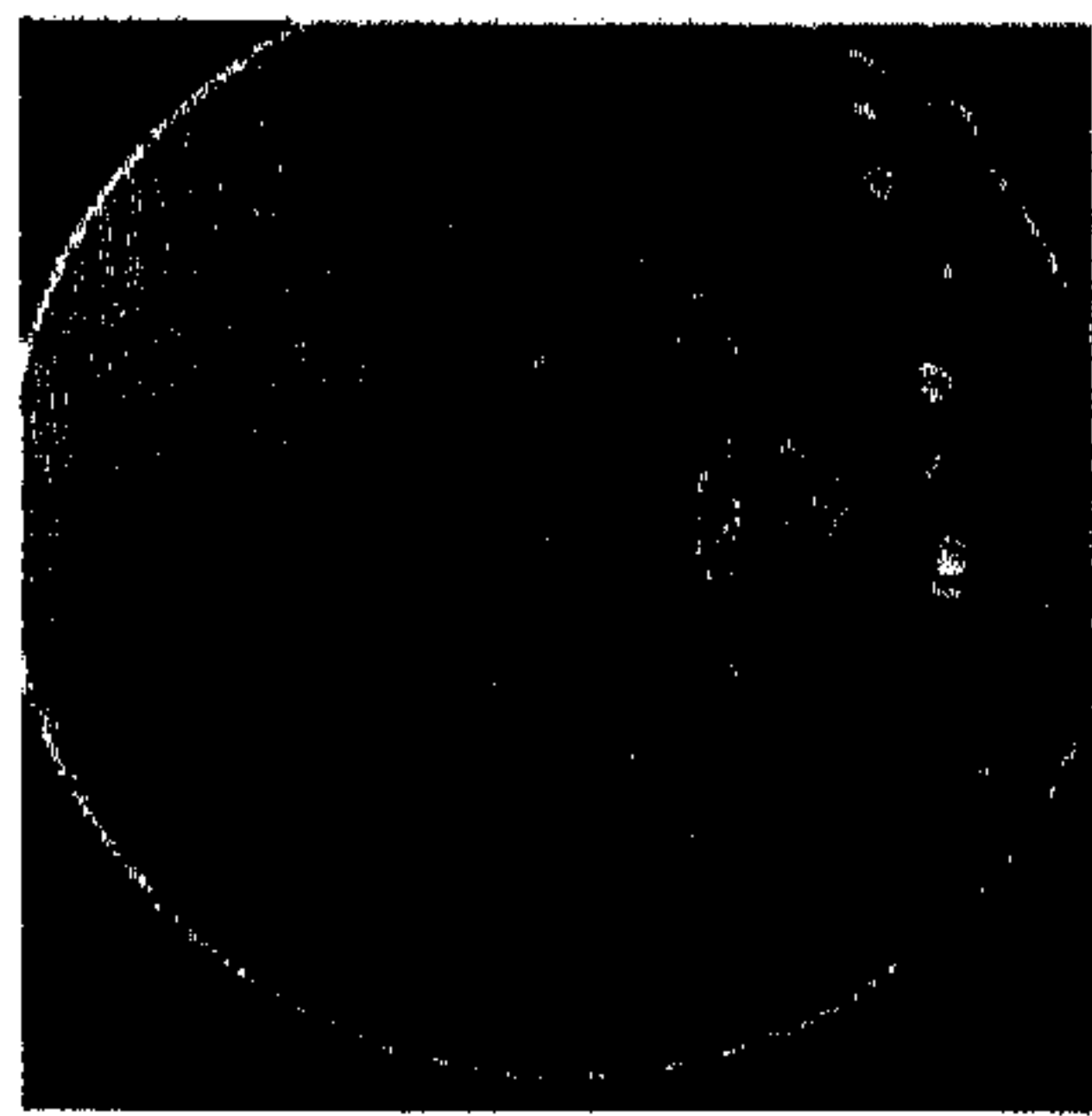


K

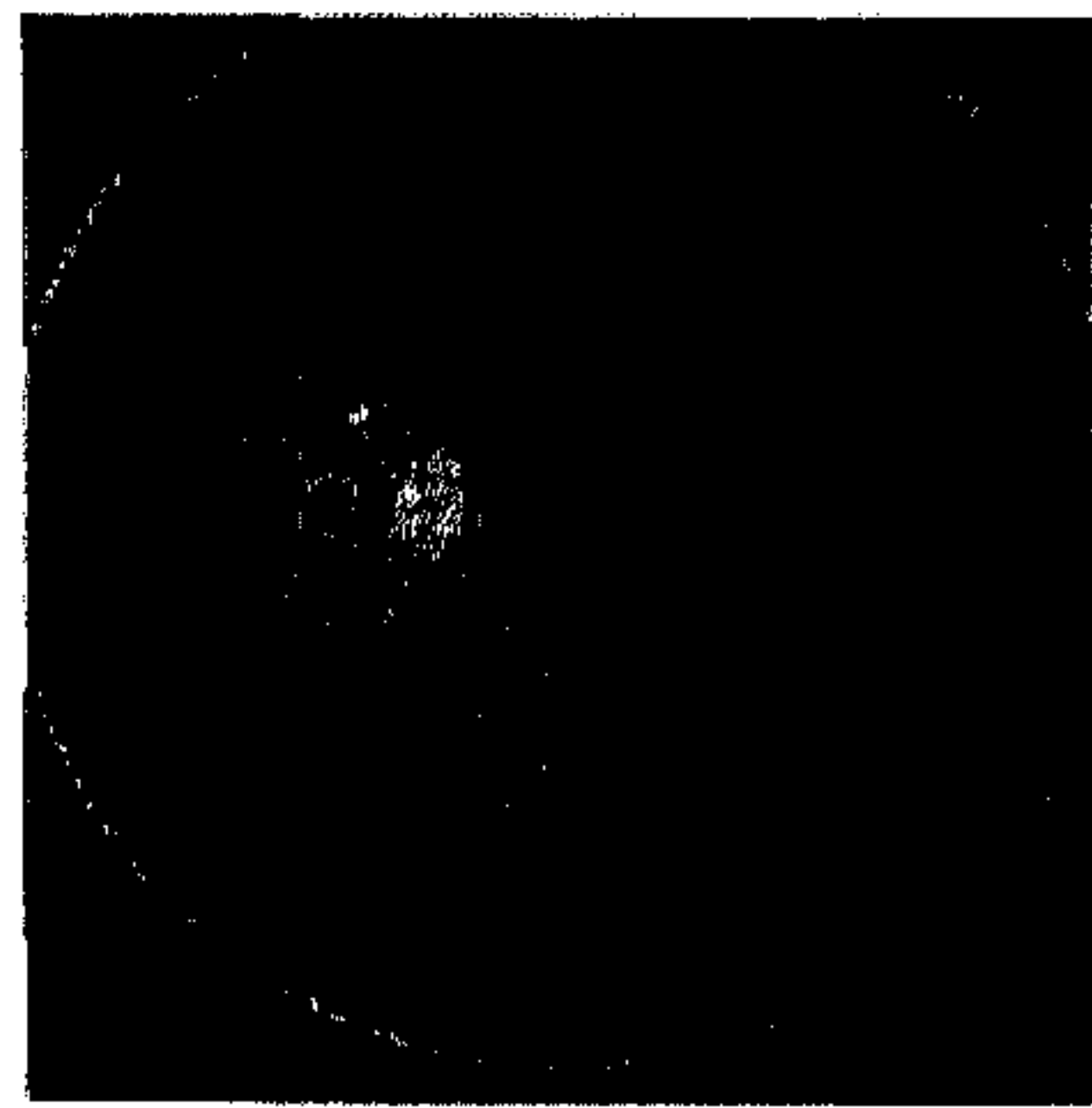


L

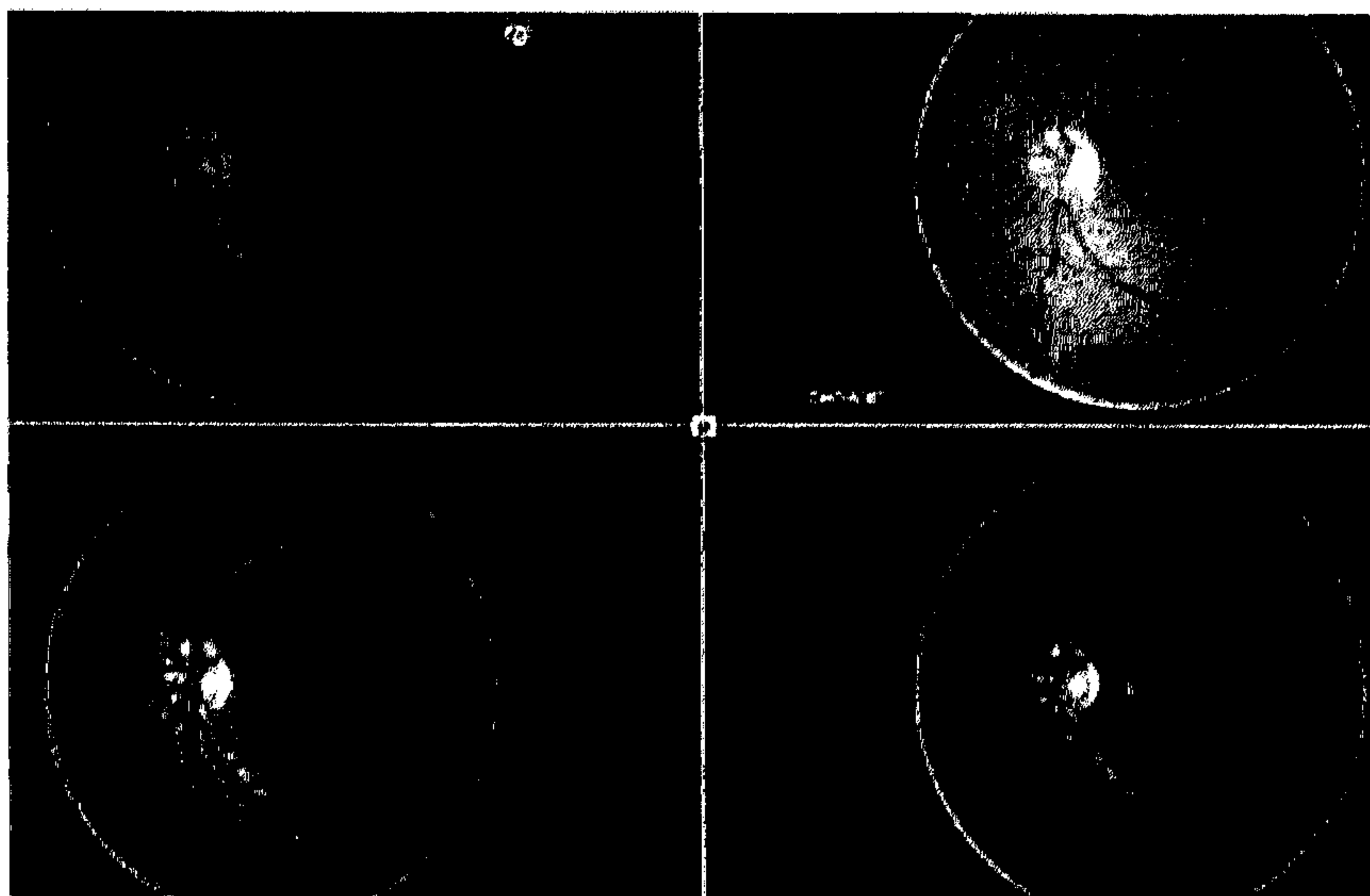
FIG. 3 (Cont'd)



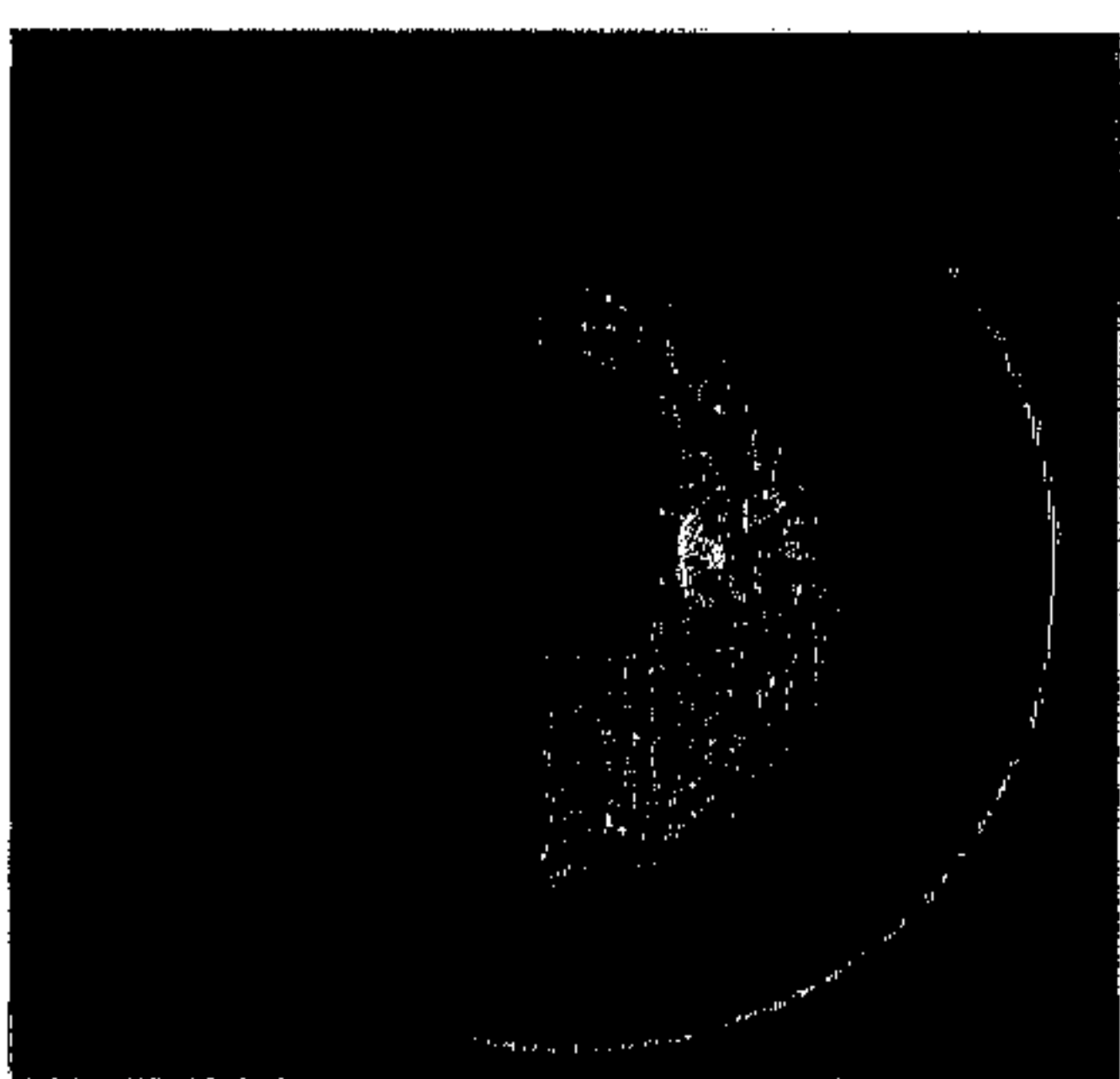
A



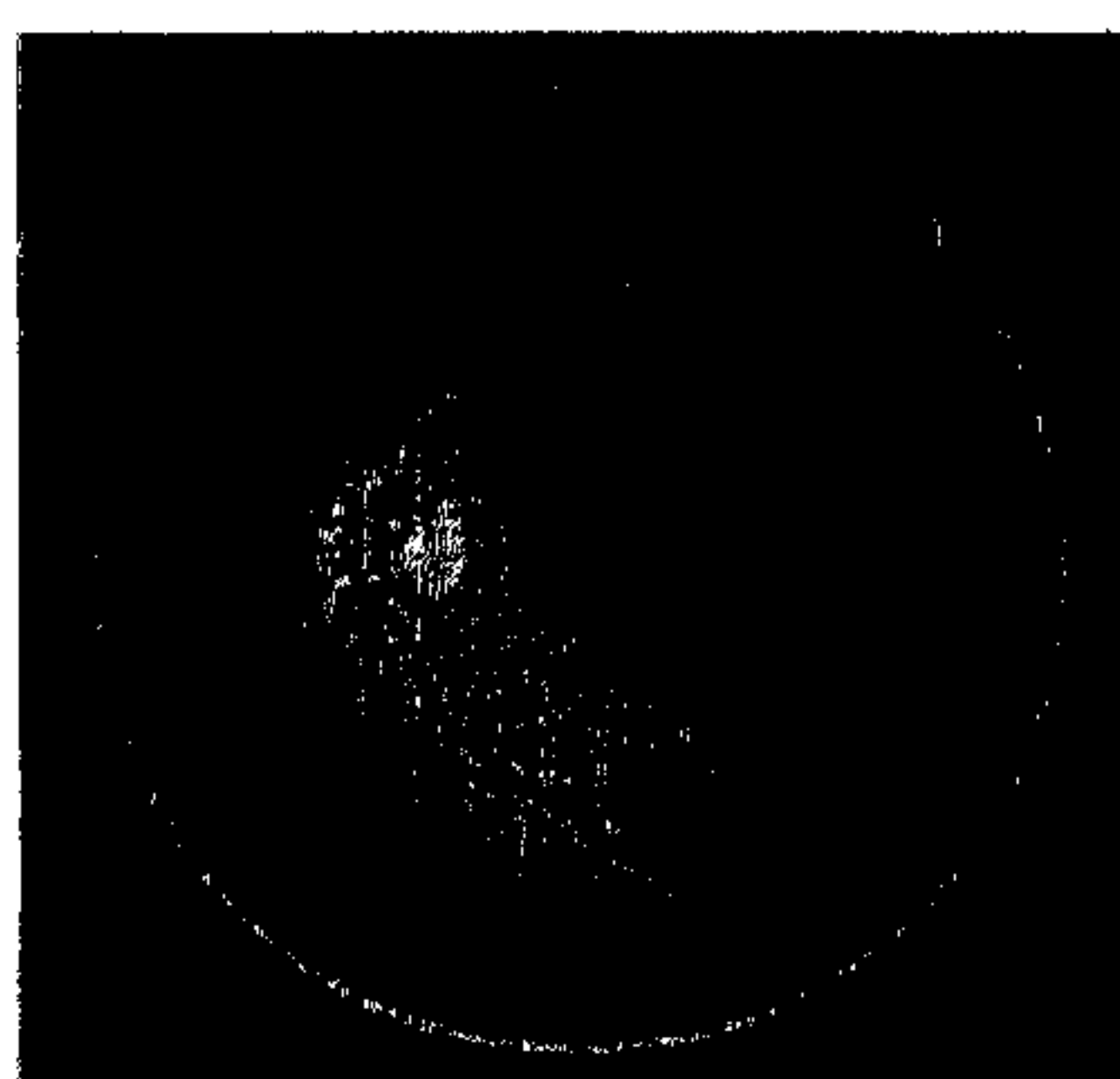
B



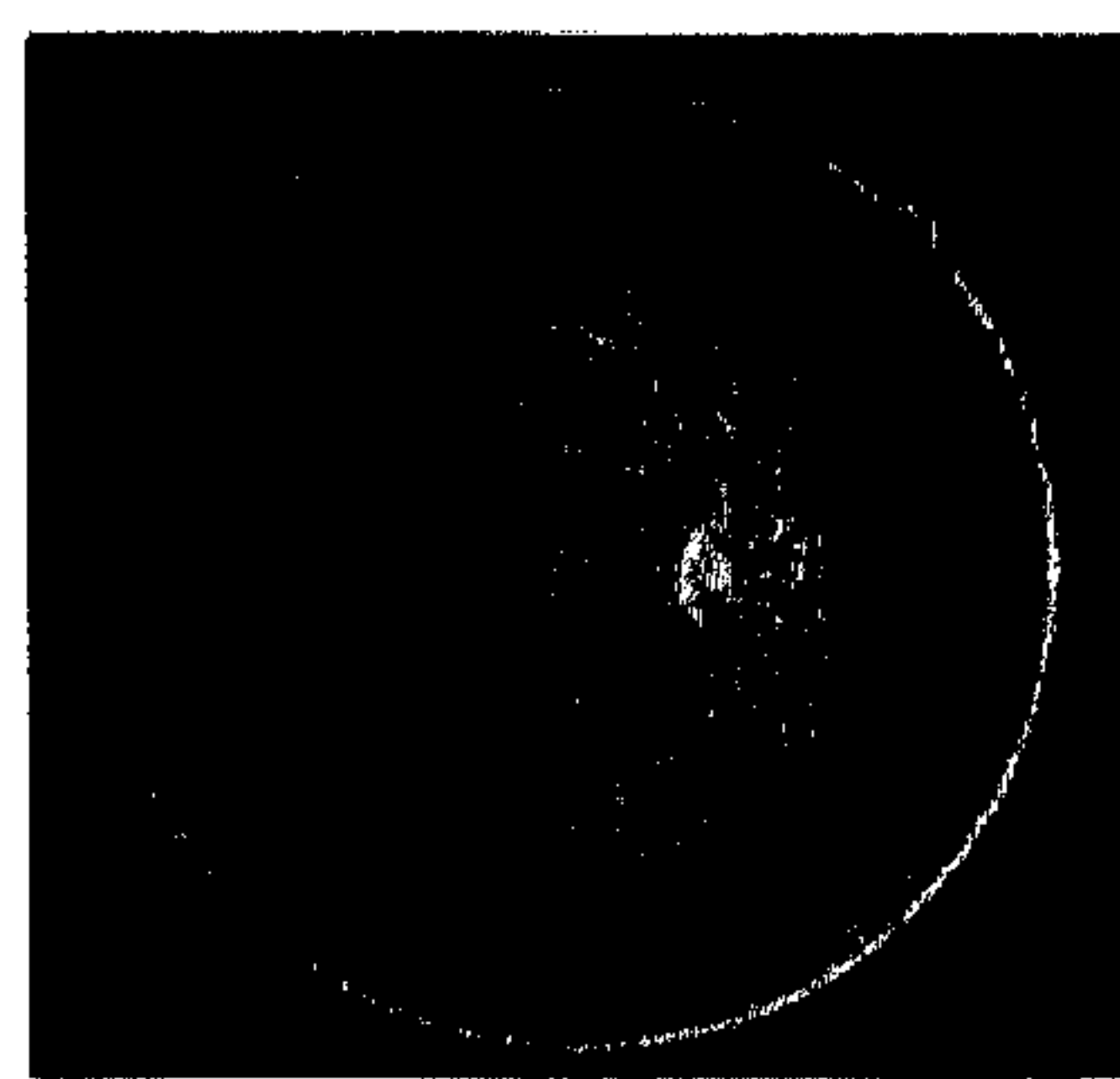
C



D



E



F

FIG. 4

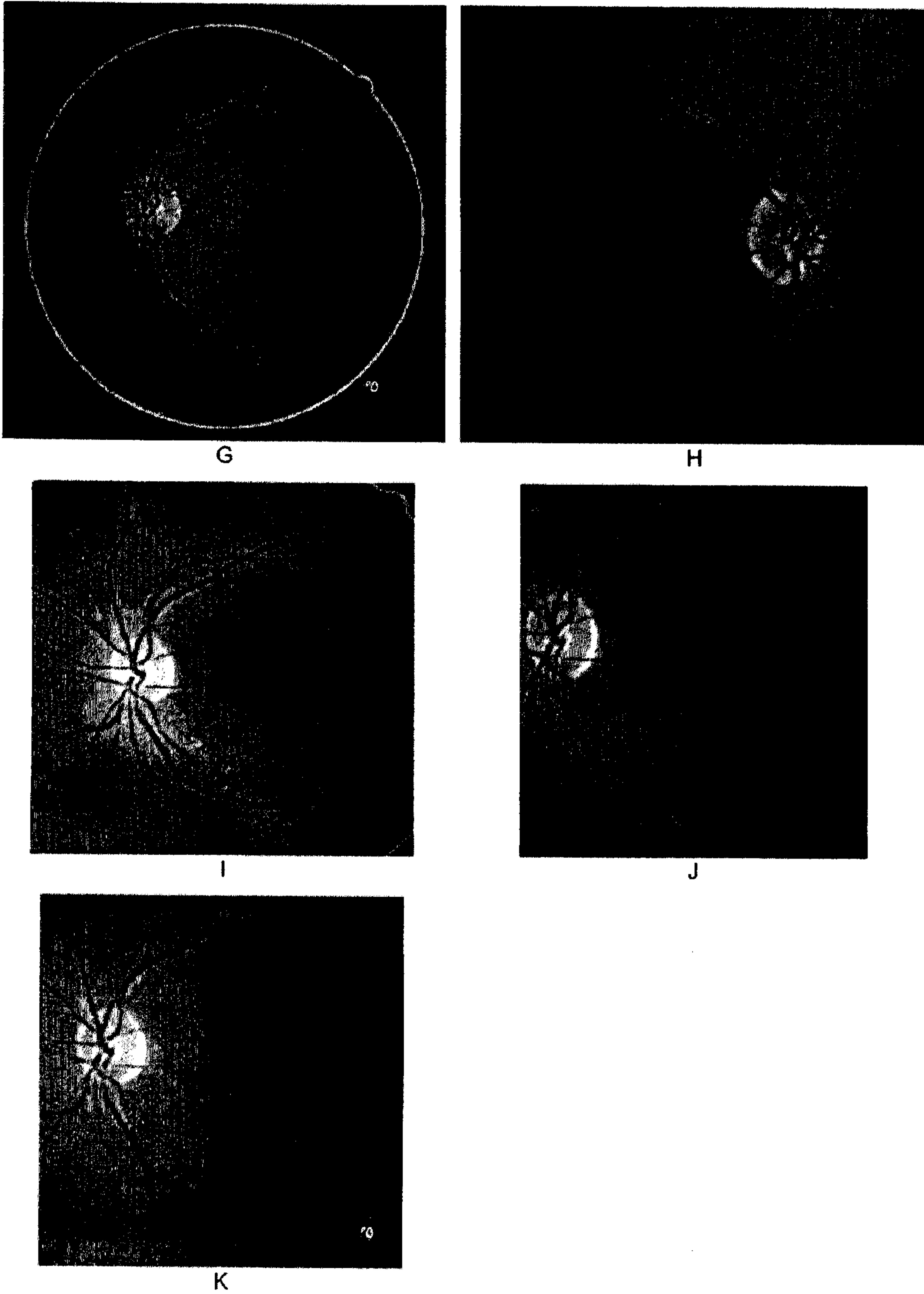


FIG. 4 (Cont'd)

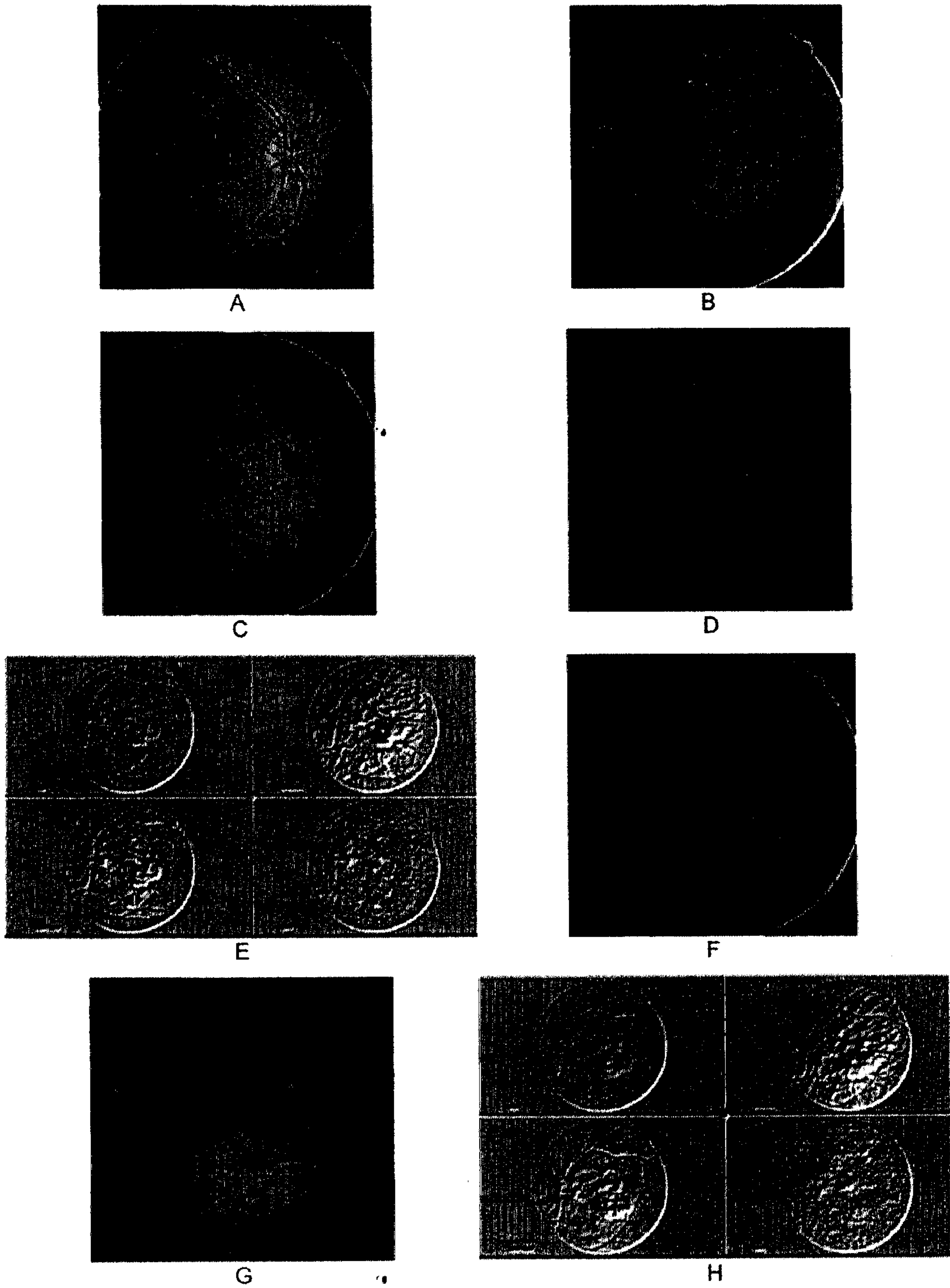
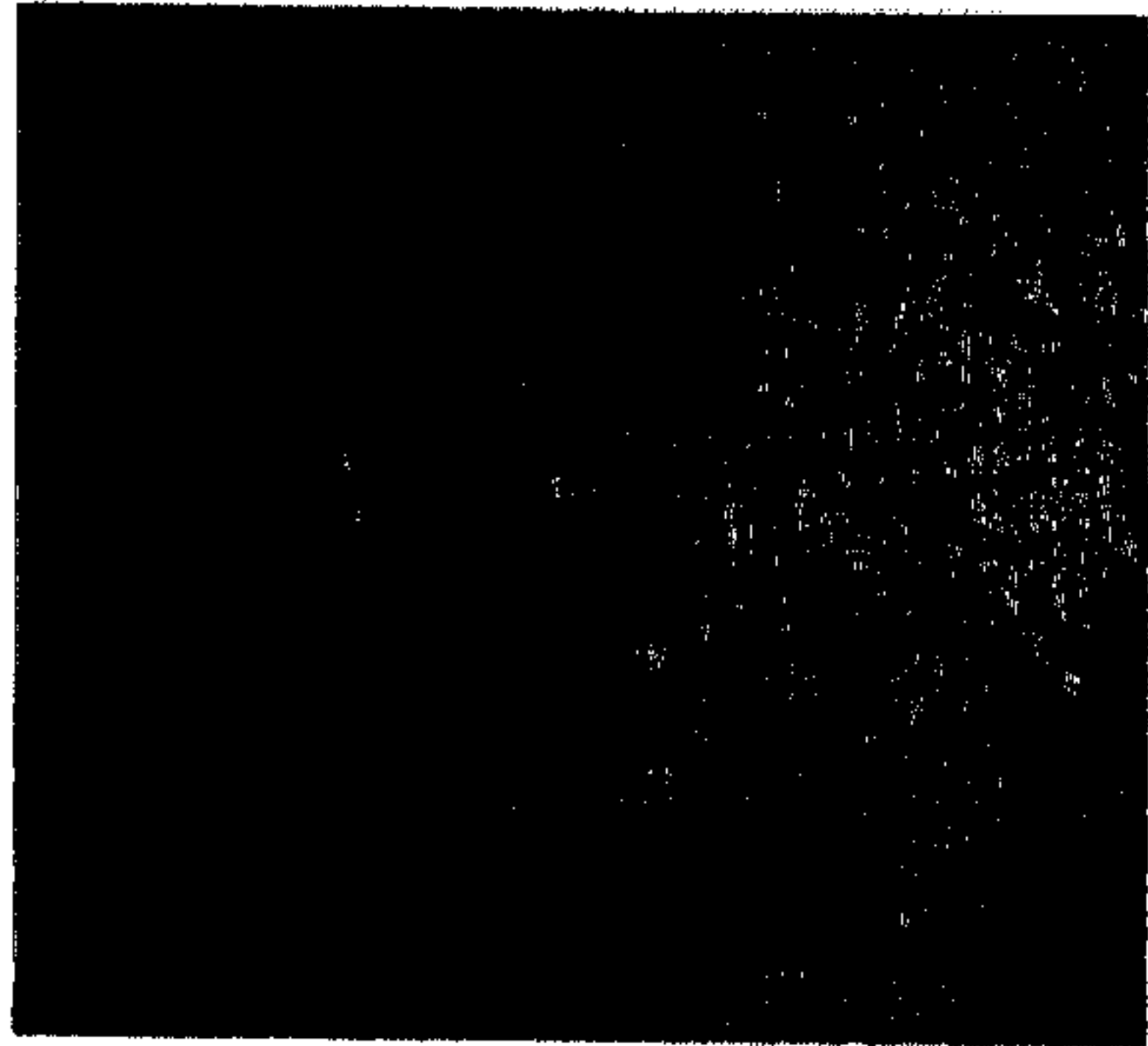
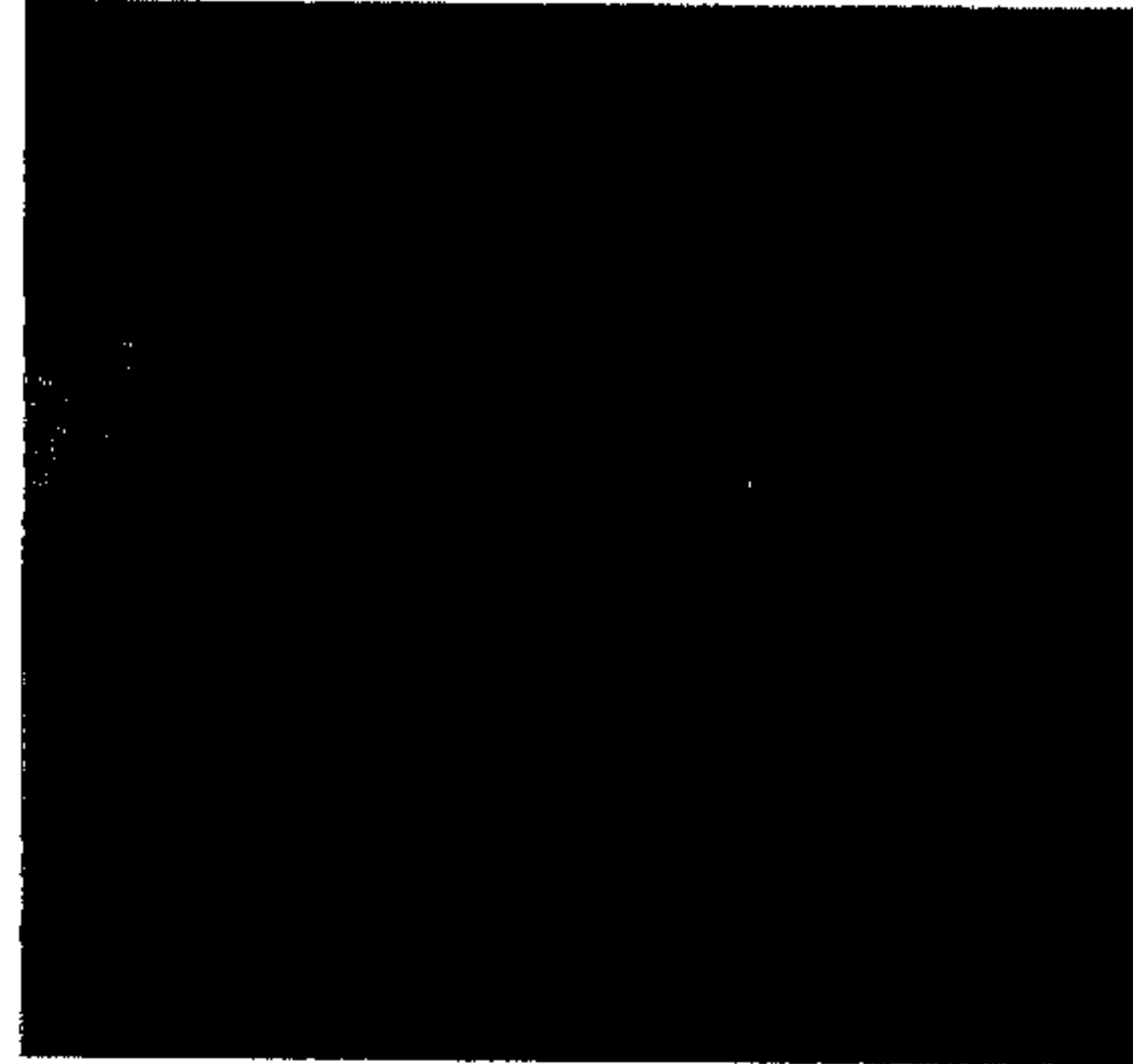


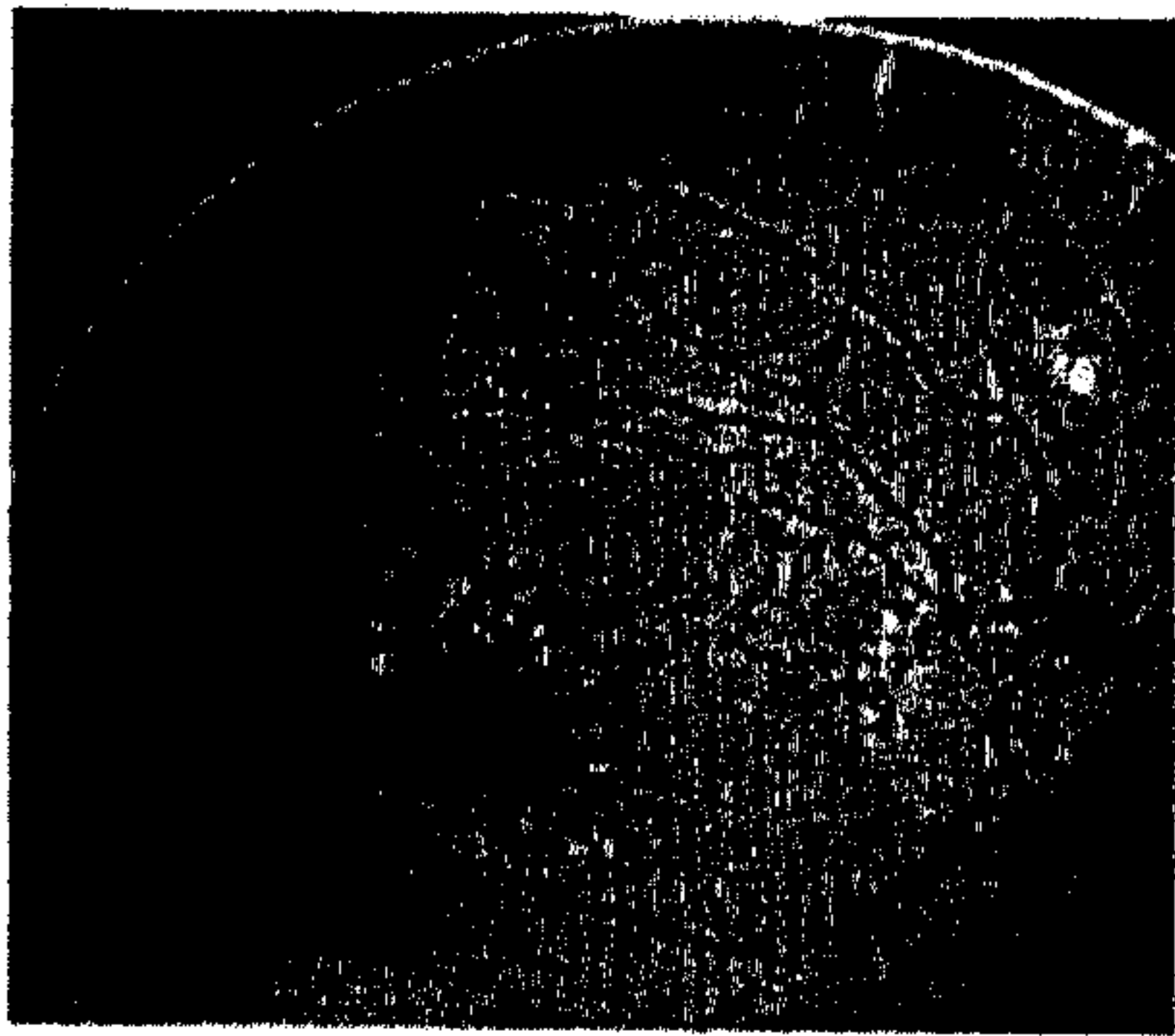
FIG. 5



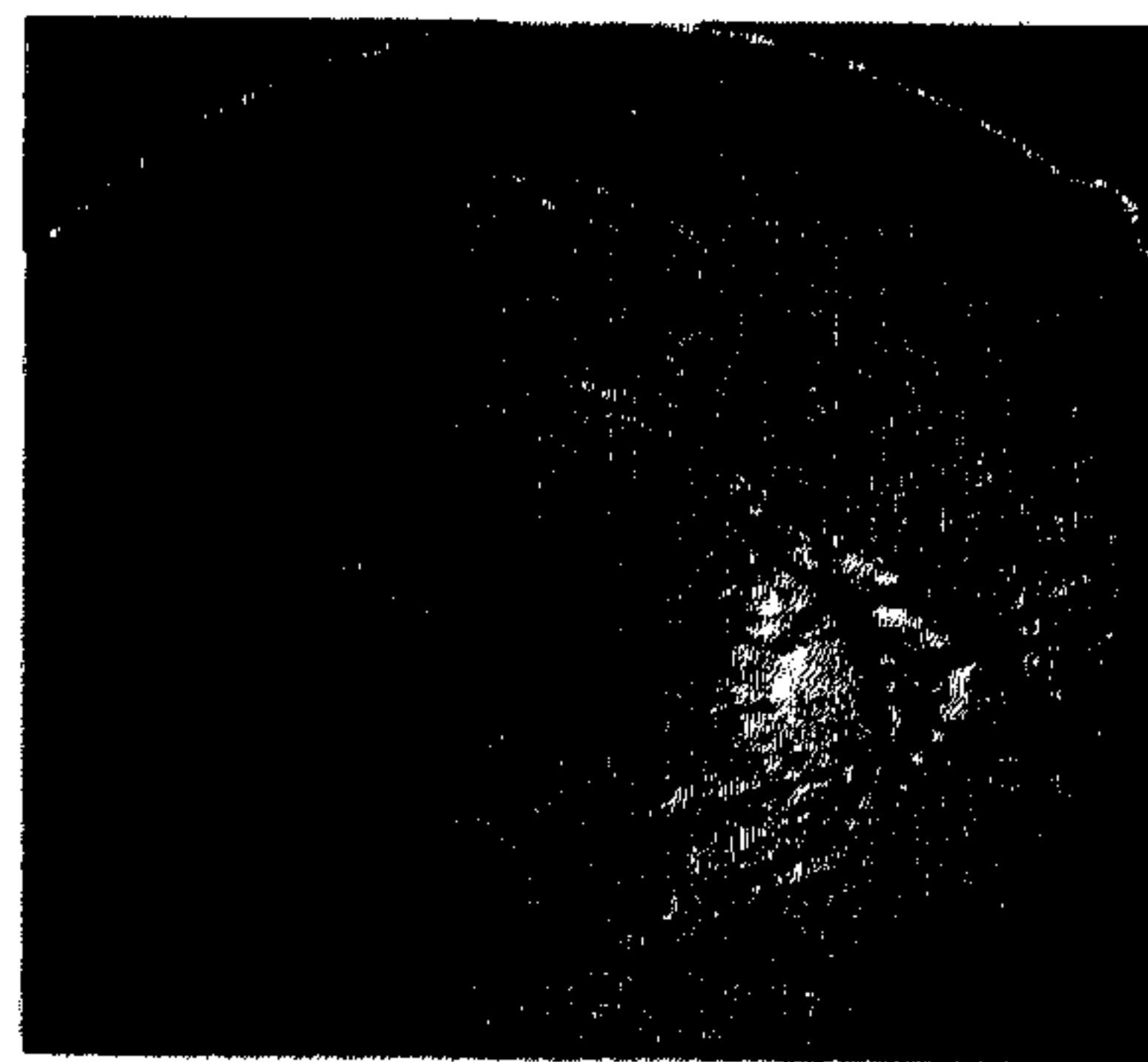
I



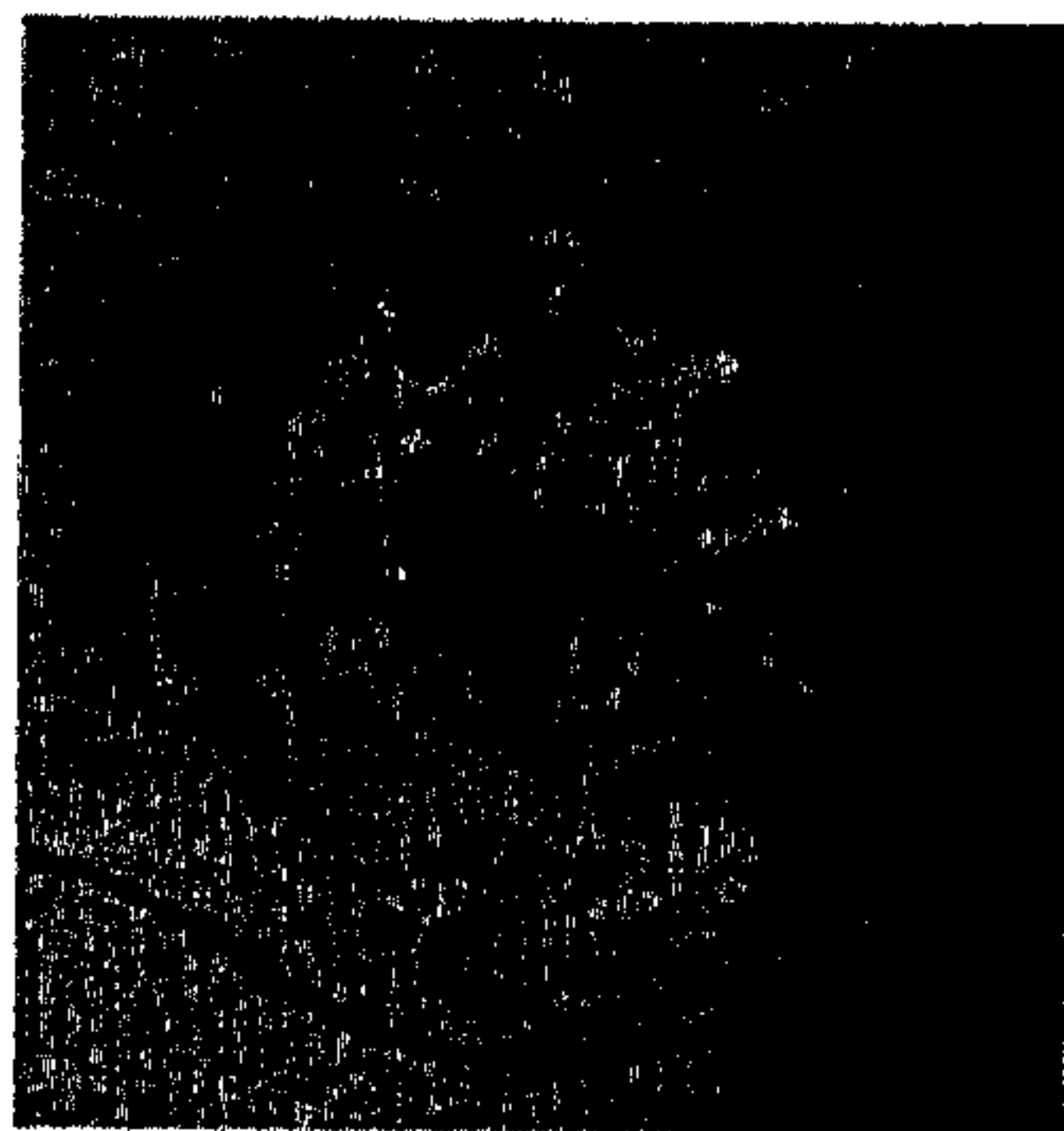
J



K



L



M

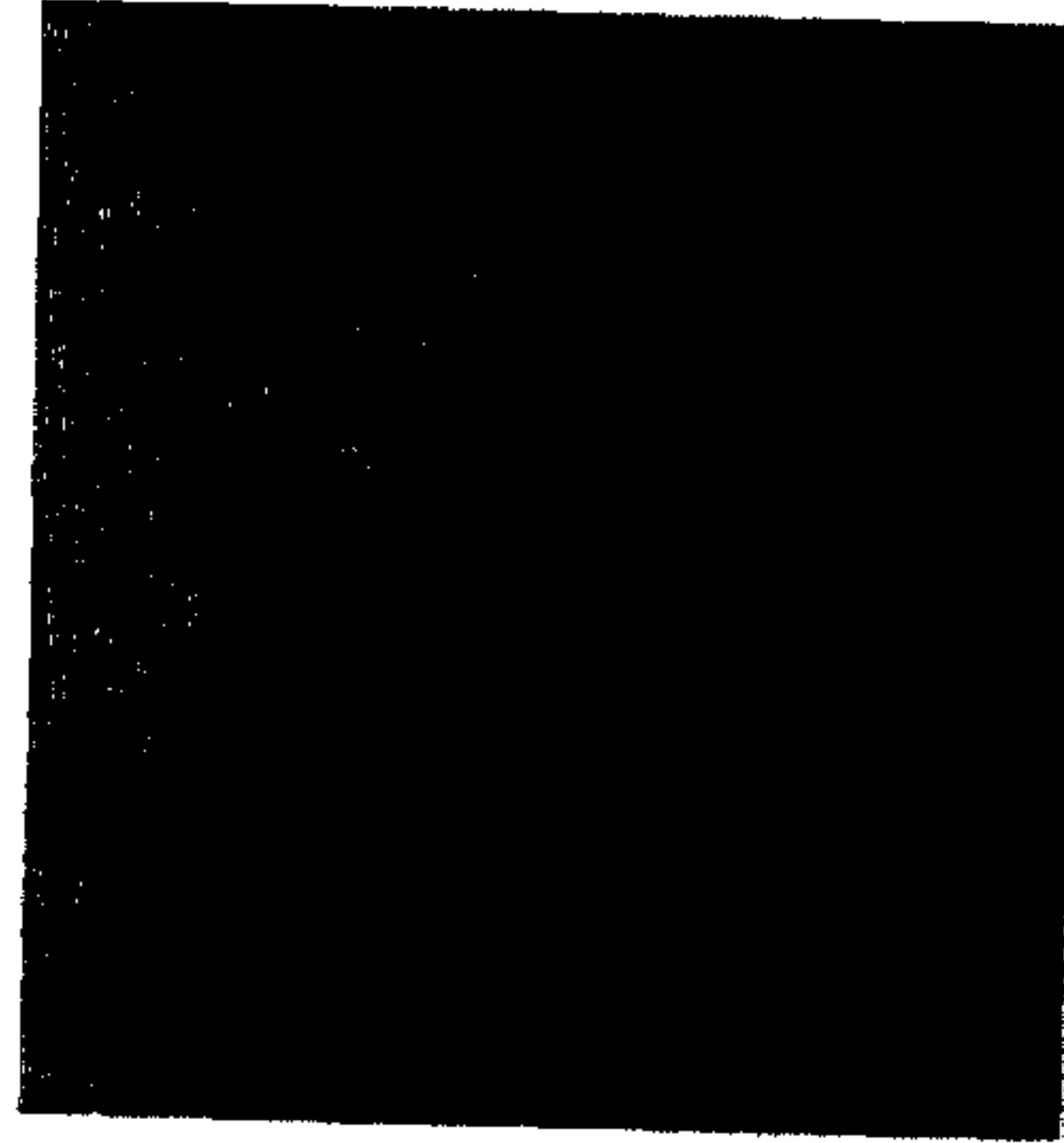


N

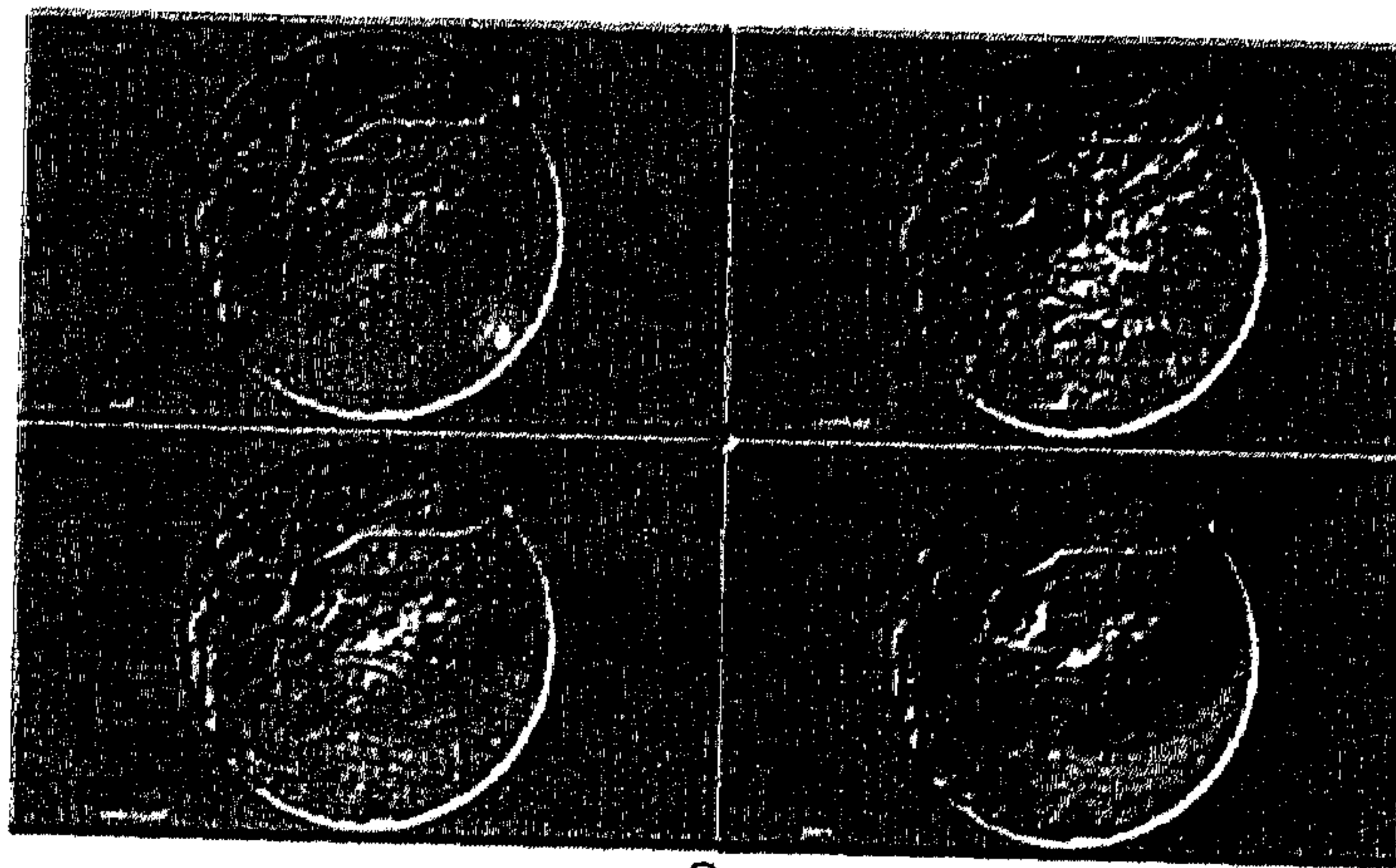
FIG. 5 (Cont'd)



O



P



Q

FIG. 5 (Cont'd)

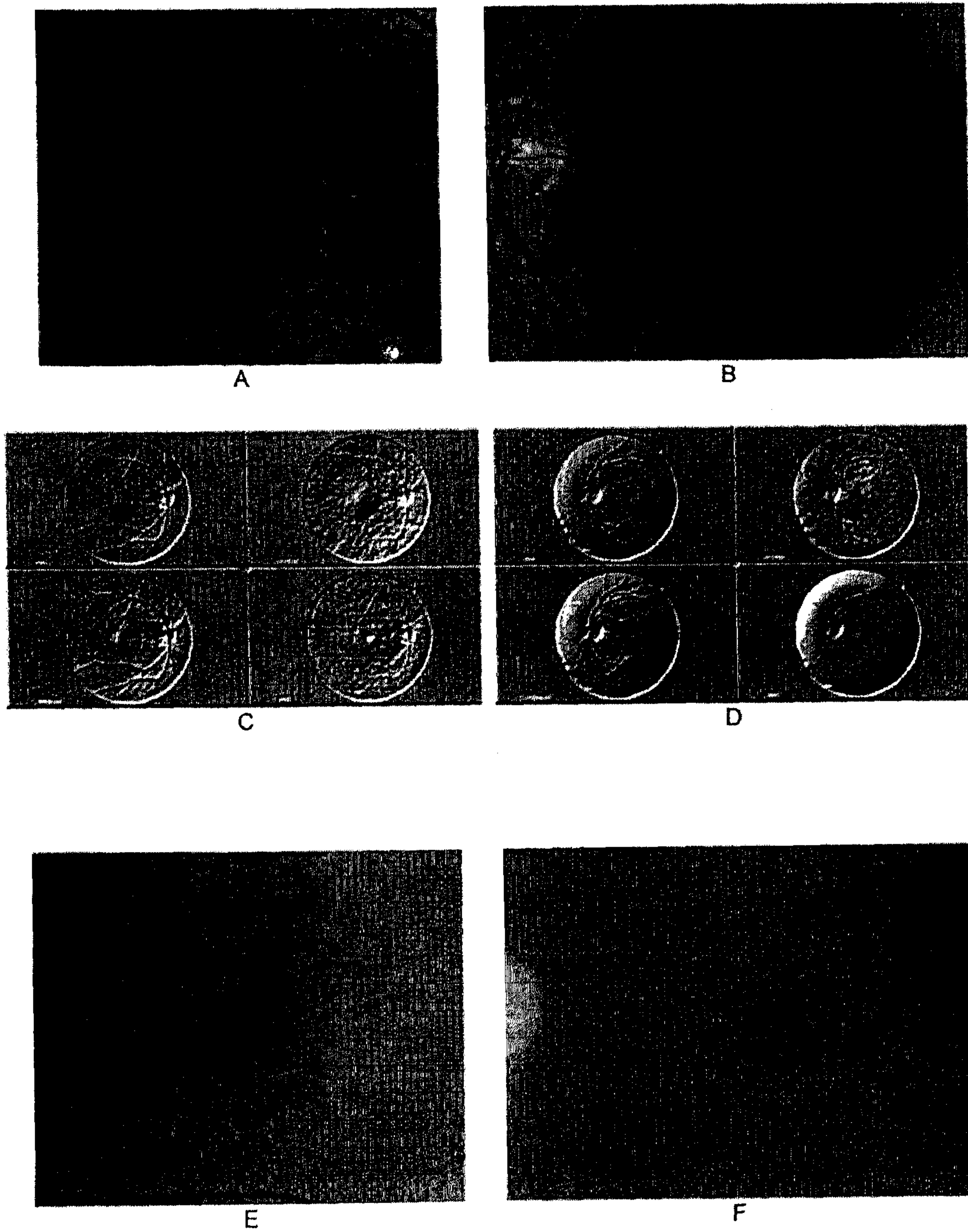


FIG. 6

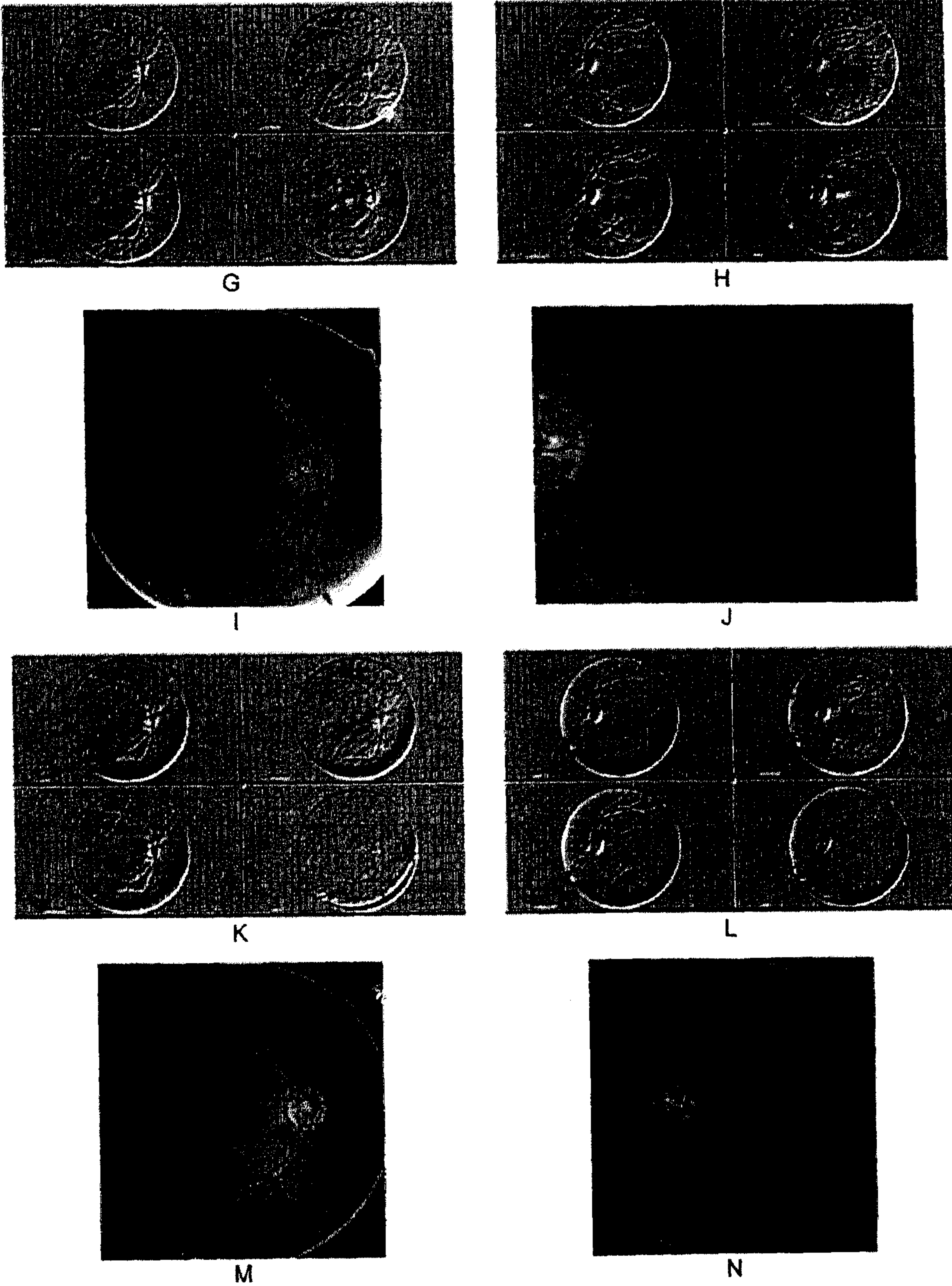
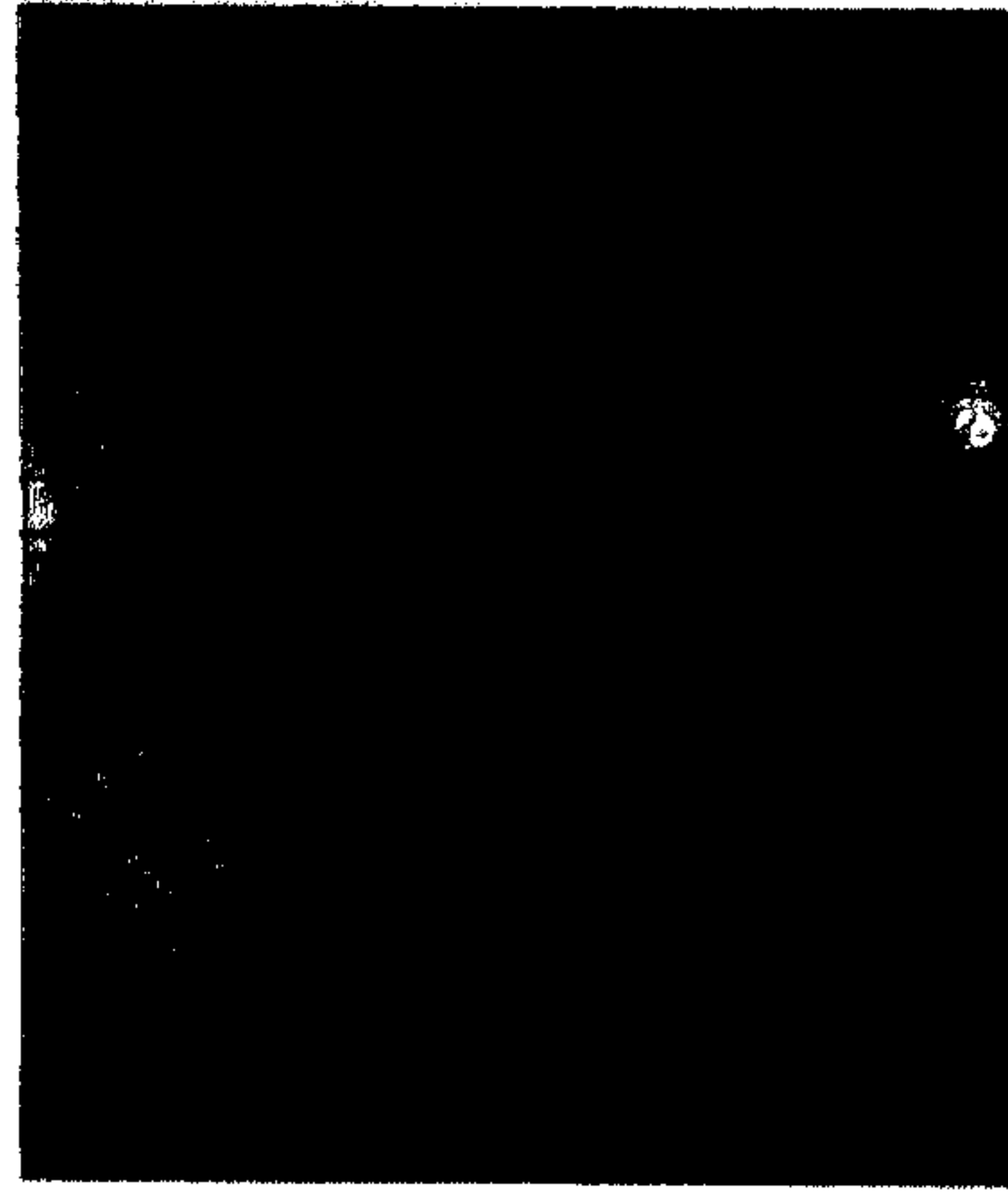
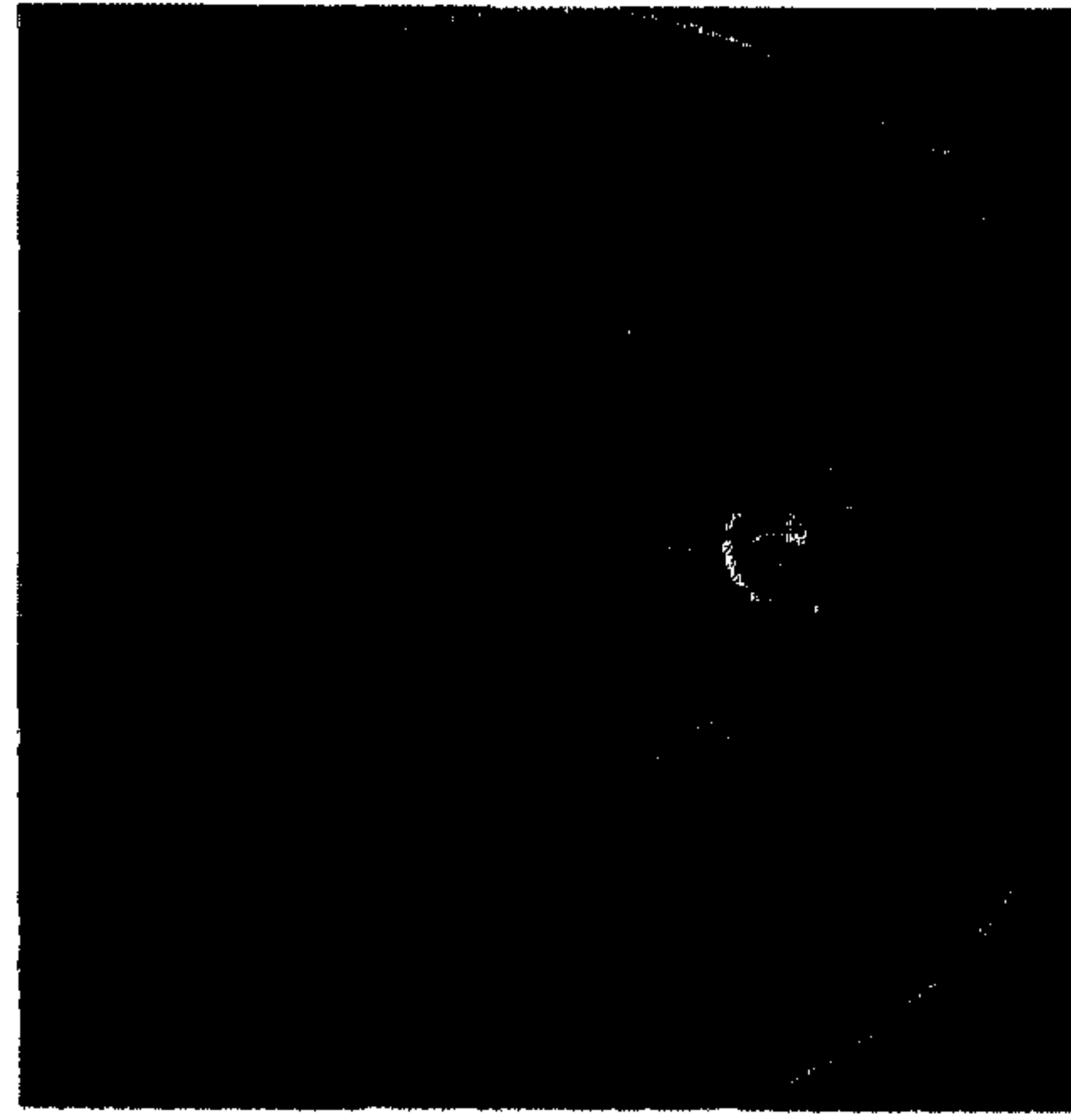


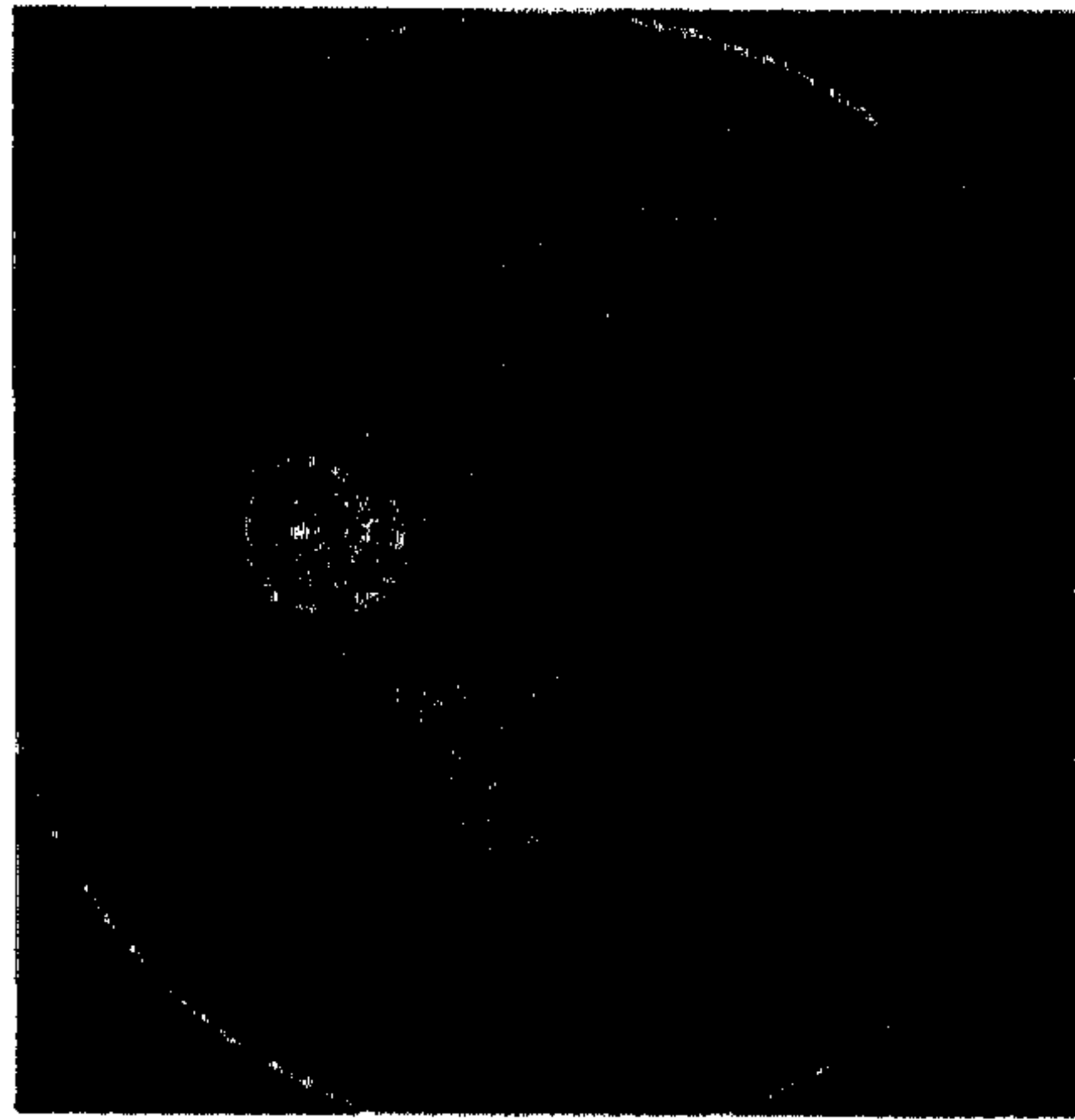
FIG. 6 (Cont'd)



O



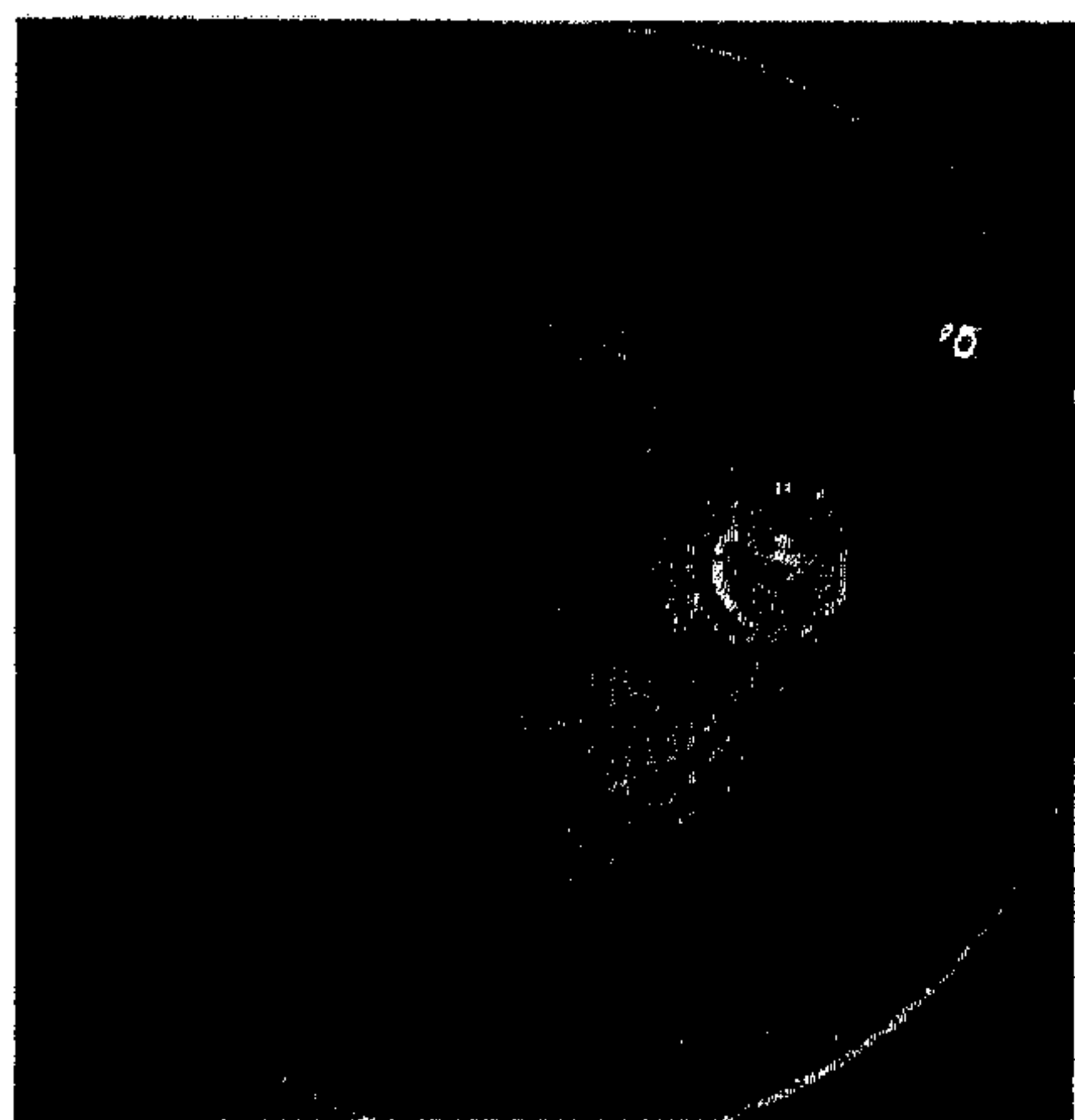
P



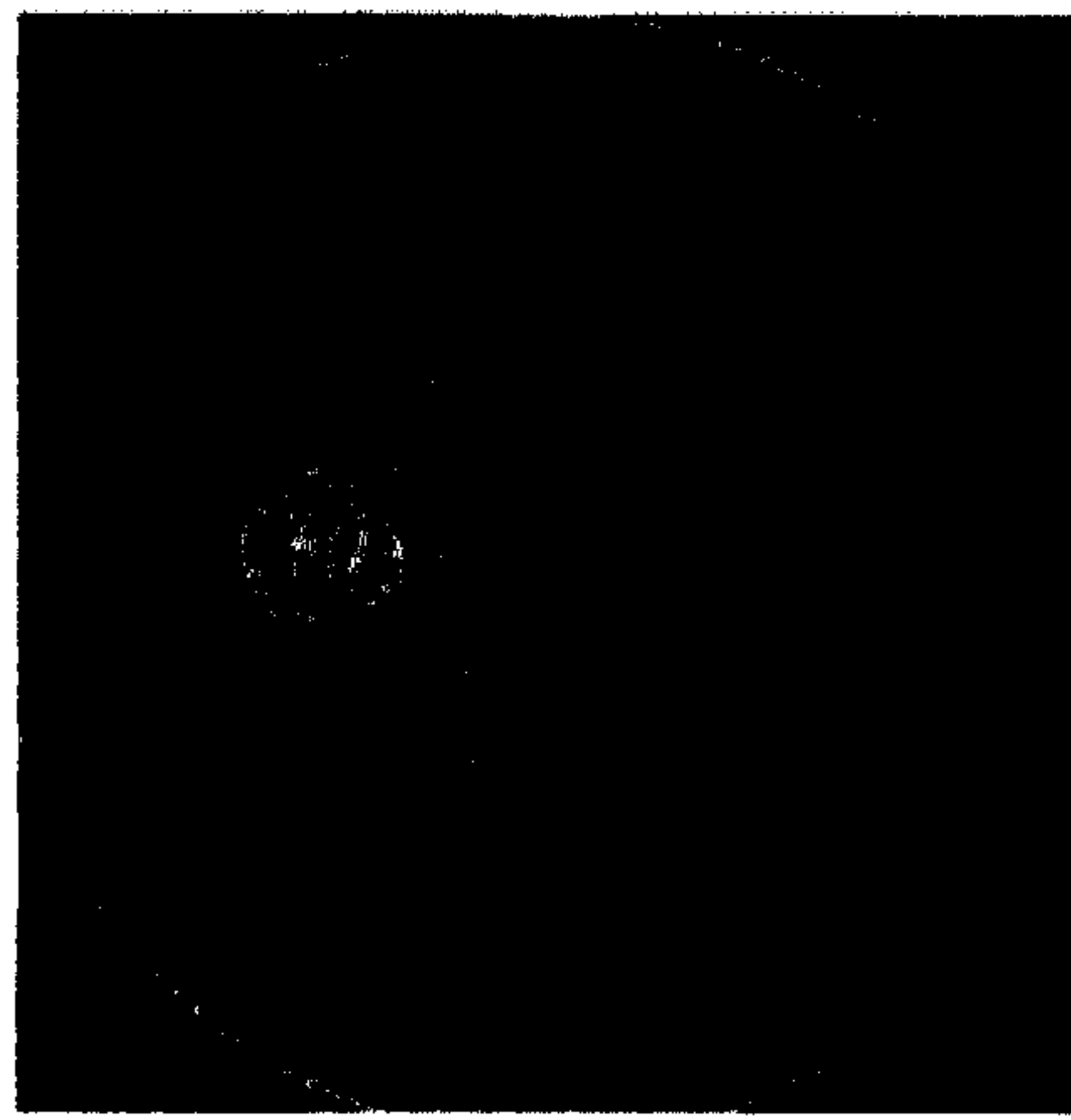
Q



R



S



T

FIG. 6 (Cont'd)

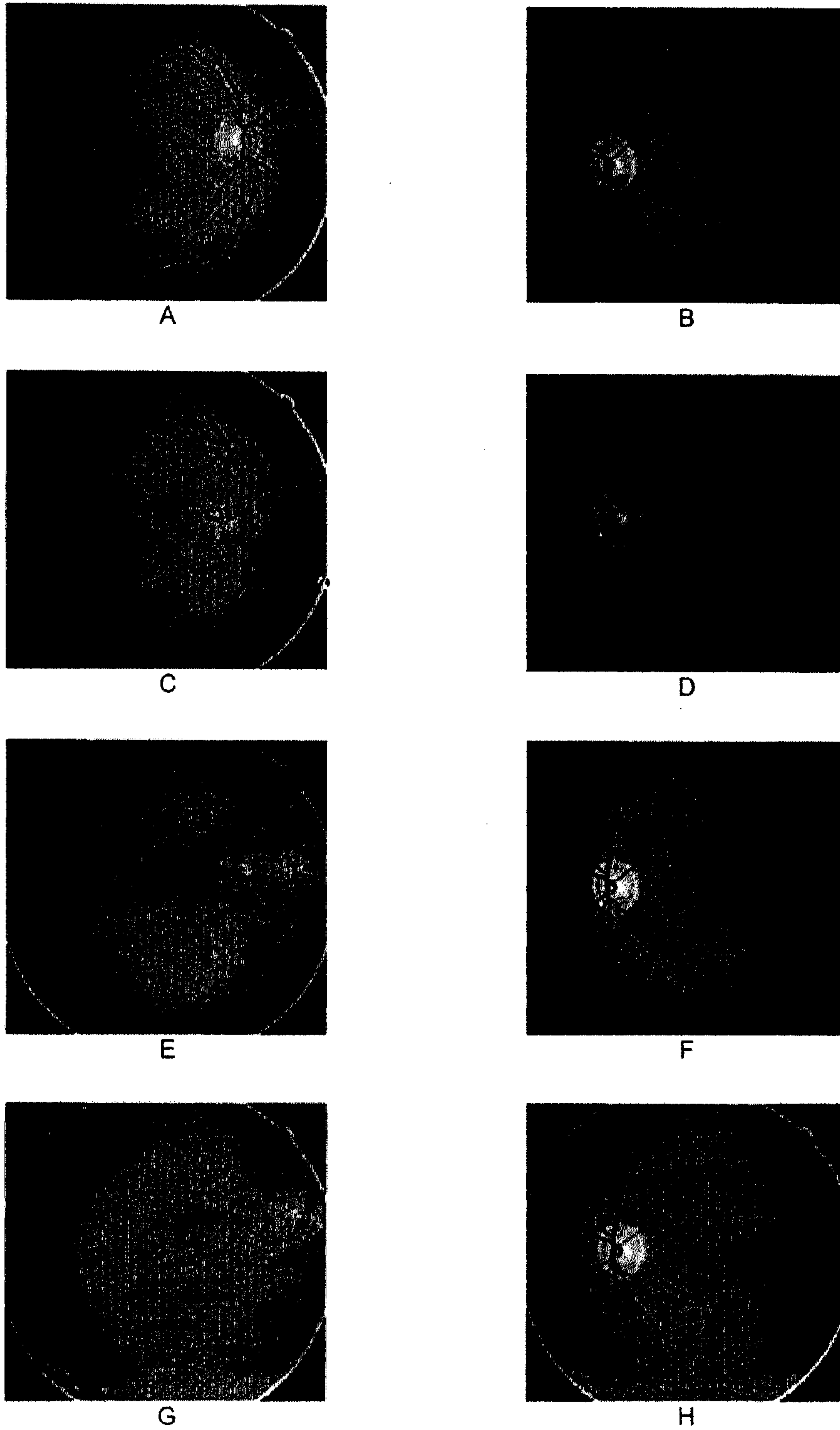


FIG. 7

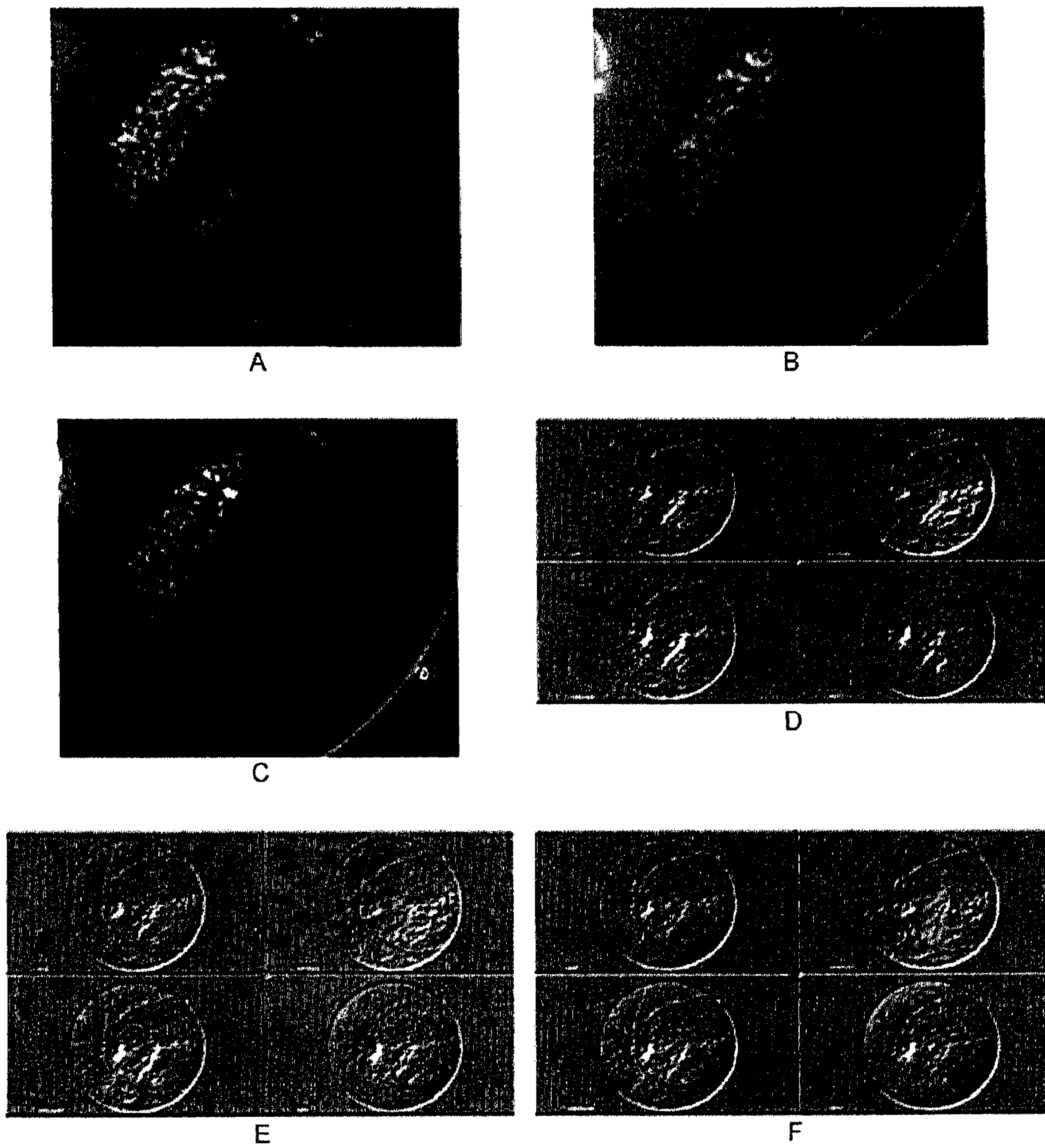


FIG. 8

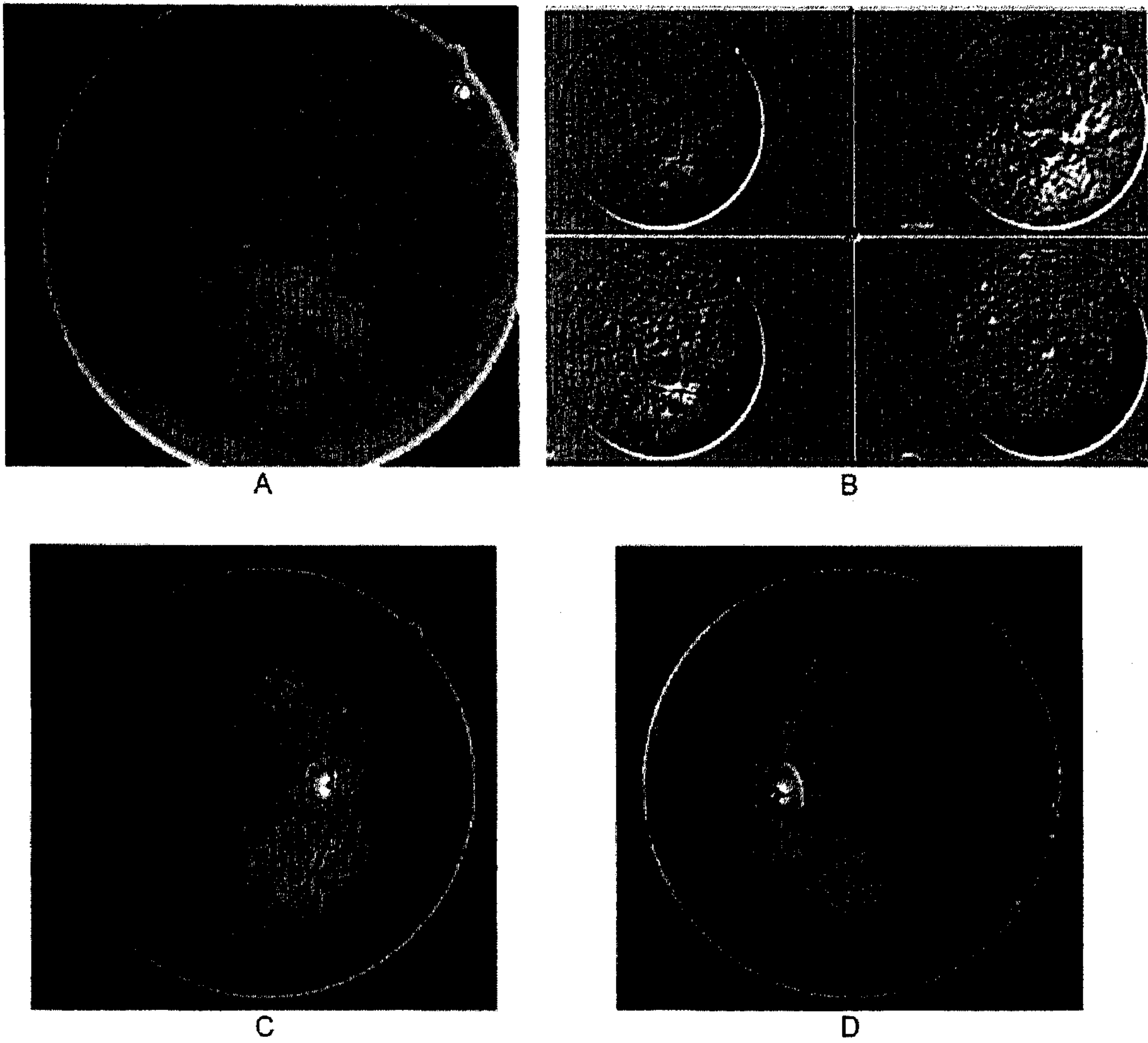
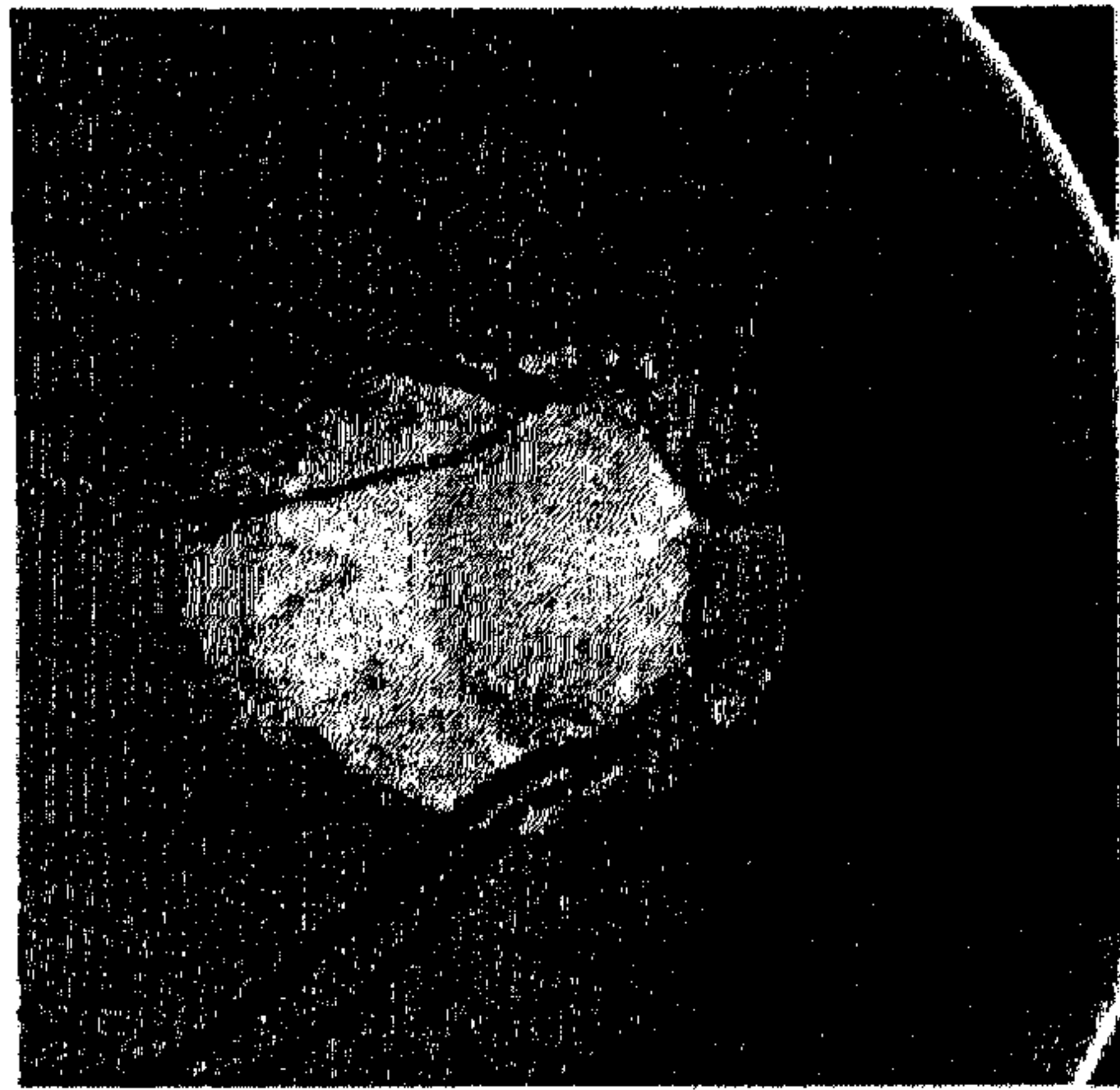


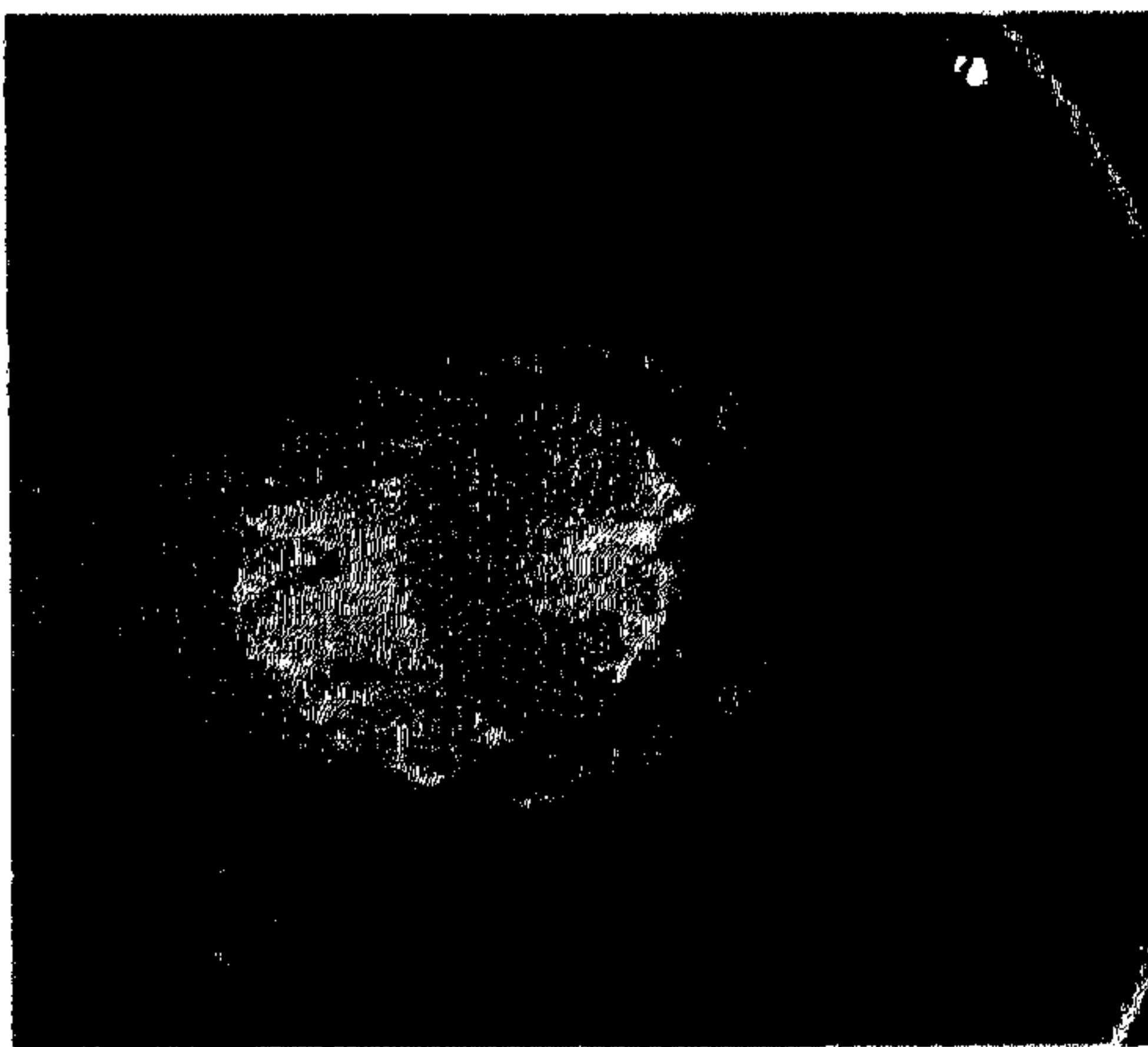
FIG. 9



A



B



C



D

FIG. 10

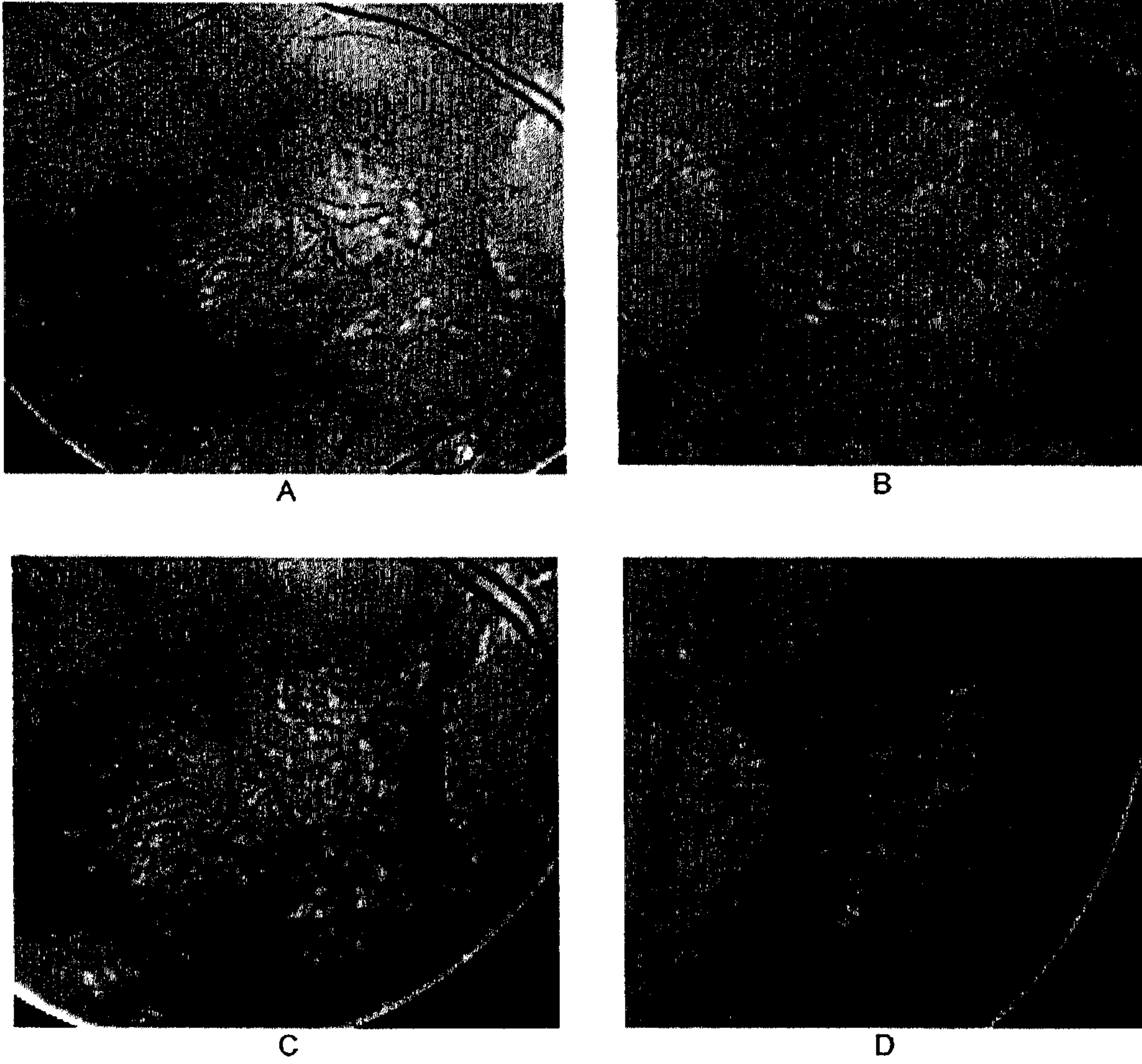


FIG. 11

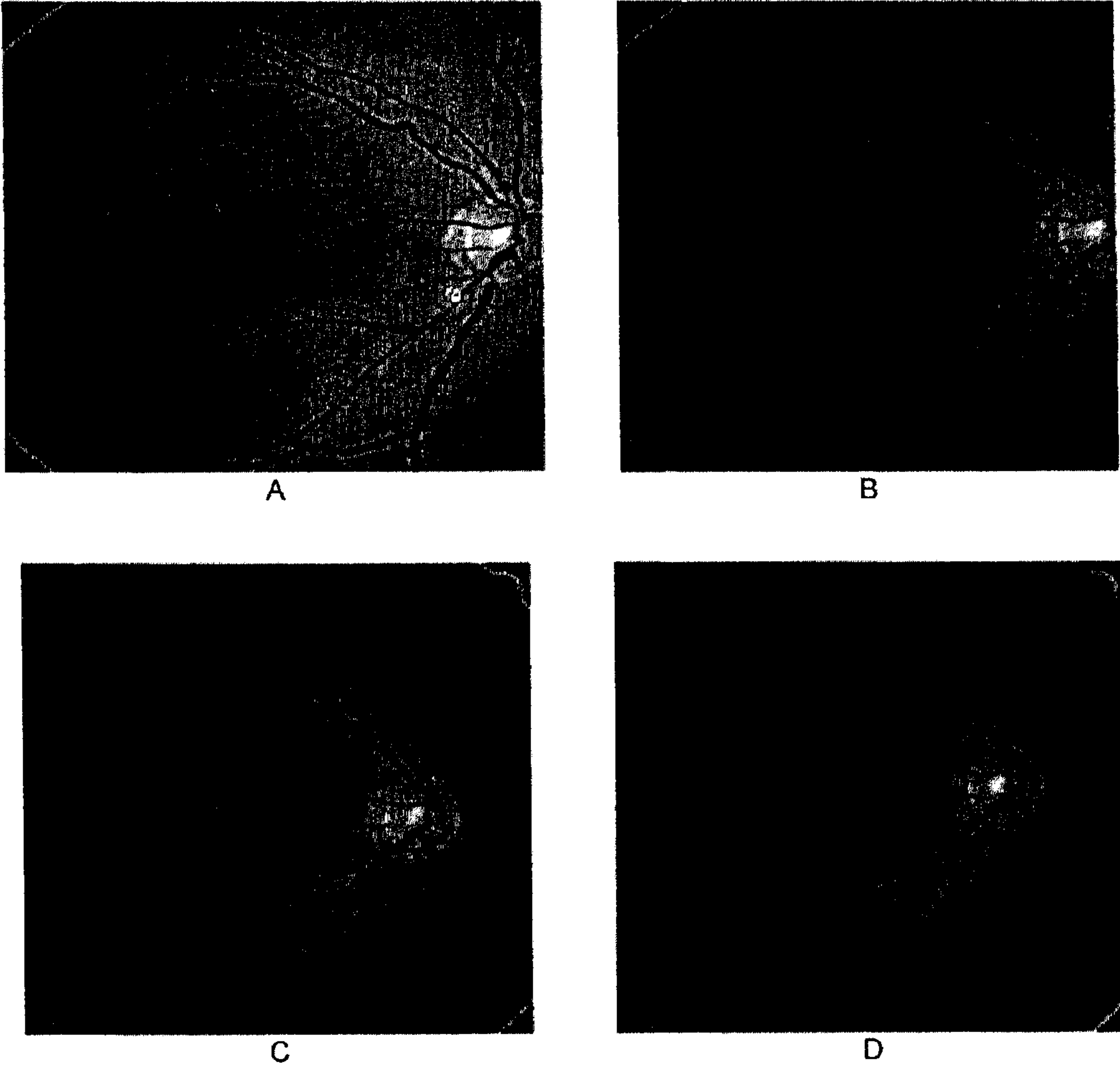


FIG. 12