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CARBONATE-HYDROXYLAPATITE, HOPEITE, AND PARASCHOLZITE IN FIBROUS CAPSULES SURROUNDING SILICONE BREAST IMPLANTS*

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ABSTRACT

The presence of mineral matter was observed in 13.5% of the capsular tissues of 262 mammary prostheses recovered after surgical excision. Three distinct mineral phases were identified: carbonate-hydroxylapatite, parascholzite and hopeite. The most abundant is carbonate-hydroxylapatite $Ca_5(PO_4,CO_3)_3(OH)$, a well-known physiological and pathological mineral. Parascholzite, $CaZn_2(PO_4)_2 \cdot 2H_2O$, and hopeite, $Zn_3(PO_4)_2 \cdot 4H_2O$, have not previously been reported in human tissues. The substitution of CO_3 for PO_4 in hydroxylapatite (Type B) is documented by infrared absorption spectroscopy. Statistical analysis of the data reveals links between the presence of the phosphate minerals on the one hand and the prostheses having polyester (Dacron®) fixation patches, the implant integrity, and the time elapsed since implantation.

Keywords: carbonate-hydroxylapatite, parascholzite, hopeite, breast implant, fibrous capsulas, biominerals, infrared absorption spectroscopy.

SOMMAIRE

Nous avons découvert des accumulations de matière minérale dans 13.5% des capsules fibreuses de 262 prothèses mammaires reçues après exérèse chirurgicale. Trois phases minérales ont été identifiées: hydroxylapatite carbonatée (la plus répandue), $Ca_5(PO_4,CO_3)_3(OH)$, biominéral physiologique et pathologique bien connu, parascholzite $CaZn_2(PO_4)_2 \cdot 2H_2O$ et hopéite $Zn_3(PO_4)_2 \cdot 4H_2O$. Ces deux phosphates de zinc n'avaient pas été signalés antérieurement dans les tissus biologiques humains. Les spectres d'absorption infrarouge étayent la substitution du CO_3 au PO_4 dans l'hydroxylapatite de type B. L'analyse statistique démontre un lien entre la présence des phases minérales et les prothèses ayant des sites de fixation en polyester (Dacron®), l'intégrité de l'implant, et la durée du séjour des prothèses chez les patientes.

Mots-clés: hydroxylapatite carbonatée, parascholzite, hopéite, prothèse mammaire, capsule fibreuse, biominéraux, spectroscopie d'absorption infrarouge.

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INTRODUCTION

Internal mammary prostheses are amongst the most frequently used implantable devices after sutures, dental materials and arterial prostheses (Blais 1988). More than 10,000 mammary prostheses are implanted each year in Quebec; 140,000 Canadian and more than 1,000,000 American women bear them. These prostheses are inserted for cosmetic reasons in 80% of the cases and as post-mastectomy reconstruction in the rest (Rolland *et al.* 1989).

Although short-term results seem rather good, reoperation rates can be very high; one woman out of three is a potential candidate for reoperation within ten years after implantation (Randal 1977). The principal reason for reoperation is the development of a fibrous tissue, usually called "fibrous capsule", all around the prosthesis (Fig. 1). This capsule corresponds to a normal response of the body in reaction to the foreign material implanted (Elbaz & Ohana 1982). When the capsule stays soft and thin, its presence is not a problem for the patient. In many cases, the capsule becomes thick and very contractile, the breast turns hard and painful, and reoperation is then necessary to deliver the prosthesis from this closed fibrous tissue. The other possible causes of reoperation are 1) the tear of the shell prosthesis, leading to silicone leakage, 2) the moving of the implant, resulting in deformation of the breast, and 3) the deposition of mineral matter, most commonly located on the internal surface of the capsular tissue, *i.e.*, in contact with the shell prosthesis. In an effort to prevent these evolutive complications, we have identified patients who require this type of surgery, and we have assessed and quantified the physical properties of the prostheses that may undergo changes since implantation (Rolland *et al.* 1989). It is necessary to study the pathological minerals and identify those parameters that have a significant correlation with the presence of these minerals.

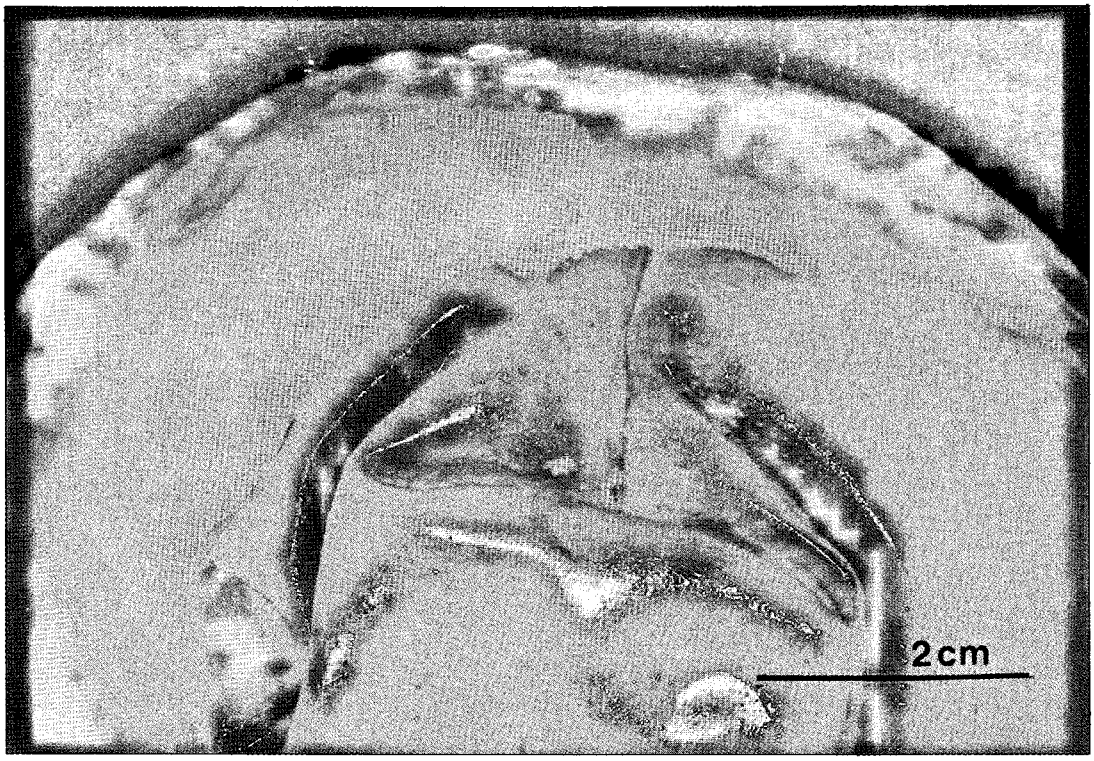

FIG. 1. A mammary prosthesis enclosed within its "fibrous capsule". Time elapsed since implantation of the prosthesis: 13 years.

TABLE 1. NUMBER OF PATIENTS, PROSTHESES, AND CAPSULES

Number of patients	176
Number of medical files available for consultation	136
Number of prostheses	262
Total number of capsules	155
Number of capsules without their prostheses	29

TABLE 2. NUMBER OF PROSTHESES FROM EACH MANUFACTURER

Manufacturer	Number of prostheses
Dow Corning	145
Heyer Schulte	64
Mme	3
Surgitek	3
Storz	3
Arion	1
Identified manufacturer	219
Non identified manufacturer	43

MATERIALS AND METHODS

The 262 mammary prostheses, some of them accompanied by their capsules, were provided by medical centres in the Quebec City area. The prostheses were explanted because of complications following implantation. All of them were composed of a silicone envelope made of polydimethylsiloxane filled with a gel of the same material. Tables 1 and 2 give the numbers of patients, prostheses, capsules, medical files consulted and the number of prostheses depending on the manufacturer. Ideally, after surgical excision, the prostheses and capsules were rinsed with physiological saline solution and fixed in 10% formaline solution without buffer or in 2% glutaraldehyde solution with a phosphate buffer. Before our investigation of the minerals deposited, the organic matter was removed by immersion in successive baths of sodium hypochloride (20%) and the materials rinsed with distilled water.

The frequencies, sizes, and physical properties of the deposits of mineral matter were determined by visual inspection of the fibrous capsules. The specific gravity was determined with a Berman balance.

Microscope slides of individual grains reduced to

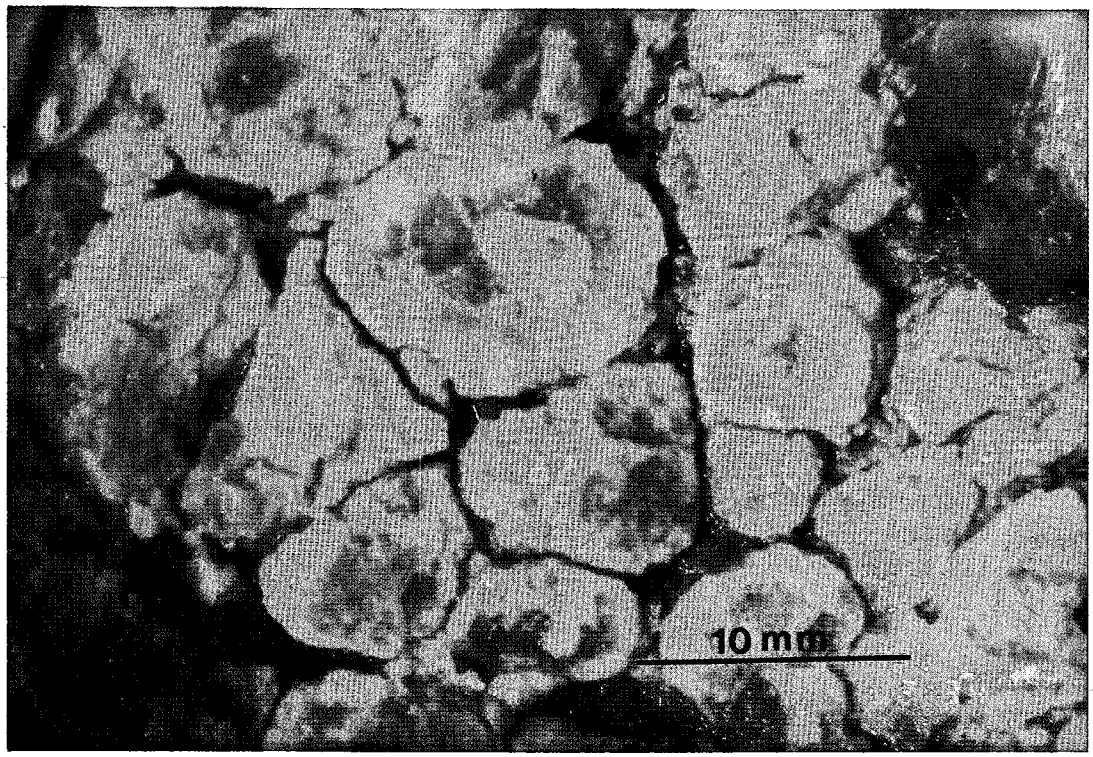

FIG. 2. Capsular tissue entirely covered with carbonate-hydroxylapatite deposits adhering to its surface on the internal side in contact with the prosthesis. Time elapsed since implantation of the prosthesis: 17 years.

30 μm were observed under a Zeiss polarizing microscope. A Philips EM300 transmission electron microscope was used in order to examine thin sections of the capsular tissues. The samples were embedded in Epon 812 and stained with uranyl acetate and lead citrate. Some carbon-covered specimens were examined by means of a JEOL JSM 35CF scanning electron microscope equipped with a Princeton Gamma Tech PGT System 4 multichannel energy-dispersion spectrometer.

A 114.6-mm Gandolfi camera was used to record X-ray-diffraction lines. The samples were exposed during twelve hours. A copper target (Cu$K\alpha$ radiation, λ 1.5418 Å) and a nickel filter were used with a Philips PW1010 generator operated at 40 kV and 20 mA. The infrared absorption spectra of pressed specimens into KBr (200 mg of KBr for 2 mg specimen) were recorded with a Beckman spectrophotometer (4000 to 400 cm^{-1}).

Three statistical tests were used to analyze the data: the Kruskal–Wallis and the Wilcoxon rank-sum tests for continuous variables not normally distributed, and the Chi-square test, with Yate's correction, on discrete variables (Walpole 1982). All tests were based on a 0.05 level of significance.

RESULTS

The macroscopic examination revealed that mineral deposition had occurred in 21 of 155 fibrous capsules (13.5%). The volume of the deposits and the size of particles per unit area varied. Three of the capsules showed little mineral matter, nine were moderately affected, and in another nine cases mineral matter was found to cover the intire surface (Fig. 2). Generally, the deposits occur on the internal faces of the capsules, at the capsule-prosthesis interface. Two specimens exhibit mineral matter within the fibrous tissue, and one specimen shows little globular groups of radiating crystals deposited on the internal and external surfaces of the capsule.

Macroscopic examination of the mineral crusts showed three types of deposits: (1) isolated white or beige tabular deposits were present in 19 of the 155 capsule specimens. Deposits found at the capsule–prosthesis interface are very thin (from a few tenths of a mm to 1 mm), with maximum length of 10 mm. On a few specimens, crystal facets with dihedral angles were observed (Fig. 3); (2) whitish equigranular aggregates, up to 4 mm in diameter. This development occurred throughout the fibrous tissue of

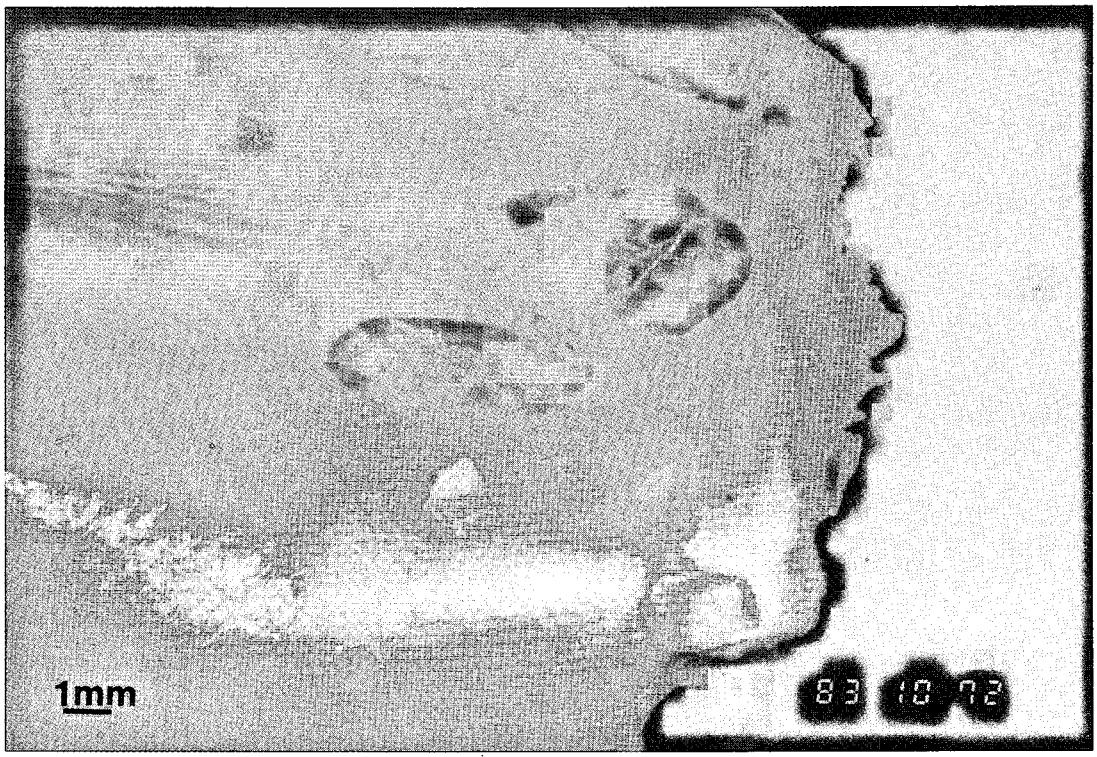

FIG. 3. Thin, tabular carbonate–hydroxylapatite showing crystal facets at the prosthesis interface of capsular tissue. Time elapsed since implantation of the prosthesis: 16 years.

two capsule specimens; (3) globular groups of radiating crystals, which grew on both surfaces of another capsule. The largest diameter of the clusters is 1 mm (Fig. 4).

The mean specific gravity of five examples of tabular deposits is 2.80, and the specific gravities of the two cases of equigranular deposits are, respectively, 2.46 and 3.22.

Transmission electron microscopy

The microscopic examination showed the presence of very small acicular crystals growing on the edge of vacuoles identified as silicone vacuoles by Zerguini (1989). The earliest crystals seemed to have grown with their longest axis perpendicular to the edge of the vacuoles (Fig. 5). At a later stage, the minerals became denser, and crystal forms were not recognizable. Finally, other crystals with encrusted facets were observed to make up the margins of the large mineralized areas.

Scanning electron microscopy and microanalysis

The tabular deposits (19 specimens) showed characteristic X-ray peaks corresponding to phosphorus and calcium, whereas in the case of massive deposits, microanalysis identified phosphorus, calcium, and zinc in one specimen and phosphorus and zinc in the other. The globular groups of radiating crystals gave characteristic X-ray peaks of phosphorus, zinc, and calcium. Observations by scanning electron microscope showed a collection of thin lamellar crystals placed in a radial arrangement (Fig. 6). The euhedral crystals and the deposits found on both surfaces of the capsule suggest that groups of radiating crystals could be artifacts. However, the capsules were conserved in glutaraldehyde solution with phosphate buffer in which the Zn ion was absent, and no other contamination was likely.

X-ray diffractometry

X-ray diffraction confirmed the identification of carbonate–hydroxylapatite, $Ca_5(PO_4,CO_3)OH$, in 19 tabular specimens. The presence of $(CO_3)^{2-}$ ions in the hydroxylapatite was indicated by a 300 reflection shifted to a higher angle (32.98° 2θ) and a 002 reflection shifted to a lower angle (25.84° 2θ) than for hydroxylapatite without carbonate (LeGeros *et al.* 1969). The main *d* values (in Å), in order of

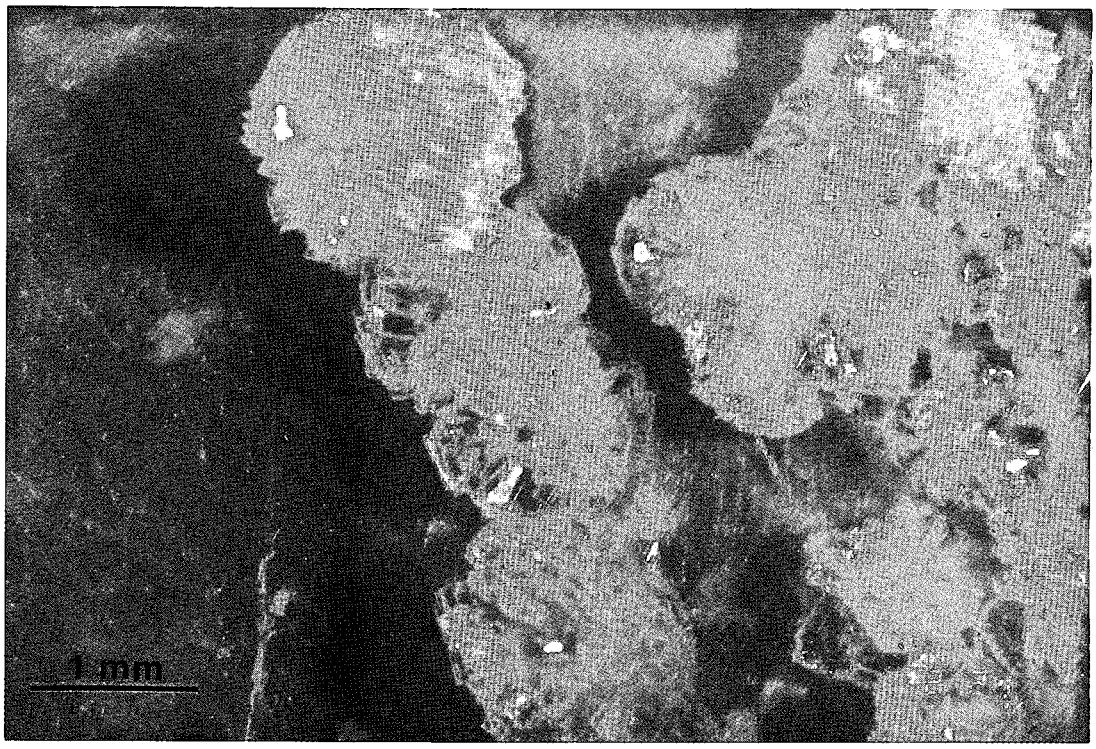

FIG. 4. Globular radiating groups of parascholzite crystals grown on the external surface of a capsular tissue. Time elapsed since implantation: 13 years.

decreasing intensity, are: 2.81, 2.78, 2.72, 3.45, 1.84, 1.94, 2.63, 2.26, 1.73, 3.07. Cell-dimension calculations based on hexagonal symmetry gave *a* 9.410, *c* 6.892 Å. These cell dimensions are consistent with those found in literature (LeGeros *et al.* 1969).

Two granular specimens from two different capsules yielded reflection values corresponding to those of parascholzite, $CaZn_2(PO_4)_2 \cdot 2H_2O$, a mineral described for the first time by Sturman *et al.* (1981). The unit cell of this phase very closely corresponds to the monoclinic subcell of scholzite. The strongest reflections *d* (in Å) are 8.57, 2.80, 4.15, 3.40, 2.77, 2.26, 4.52, 2.59.

Finally, in one of the two capsular tissues containing parascholzite, one grain provided *d* values corresponding to hopeite $Zn_3(PO_4)_2 \cdot 4H_2O$. The most intense reflections (*d* in Å) from this specimen are 2.86, 8.52, 9.16, 4.56, 3.39, 4.41, 2.27, 1.94, 2.66. The unit-cell dimensions of this orthorhombic mineral calculated from the *d* values are *a* 10.601, *b* 18.330, and *c* 5.020 Å.

Infrared absorption spectroscopy

Infrared absorption spectroscopy corroborated the identification of the three phosphate minerals and indicated, in addition to H_2O, the presence of structural CO_3. Nadal *et al.* (1970) and Bonel (1972) described two types of carbonate–apatite, named type A and type B, depending on the location of the carbonate ions in the structure. In type A, the vibration bands of the carbonate are at 1534–1465 and 884 cm^{-1}, and the carbonate ion sites are in channels along the six-fold screw axes, replacing the OH anions. In type B, carbonate vibration bands are at 1455–1430 and 864 cm^{-1}, and the carbonate groups substitute for phosphate groups in the framework. Eleven of our specimens yielded spectra representing type-B carbonate–hydroxylapatite. Frequencies and assignments for these absorption spectra are given in Table 3.

The infrared absorption spectrum of the hopeite phase described by Hill & Jones (1976) showed four bands characteristic of phosphate, but in our samples, the second lattice vibration band is missing, probably because of the low resolution of our spectrometer. The spectrum of parascholzite was interpreted and compared with that of hopeite. Frequencies and band assignments for these two spectra are given in Table 4. Three more specimens yielded spectra consistent with a mixture of carbonate-hydroxylapatite and parascholzite.

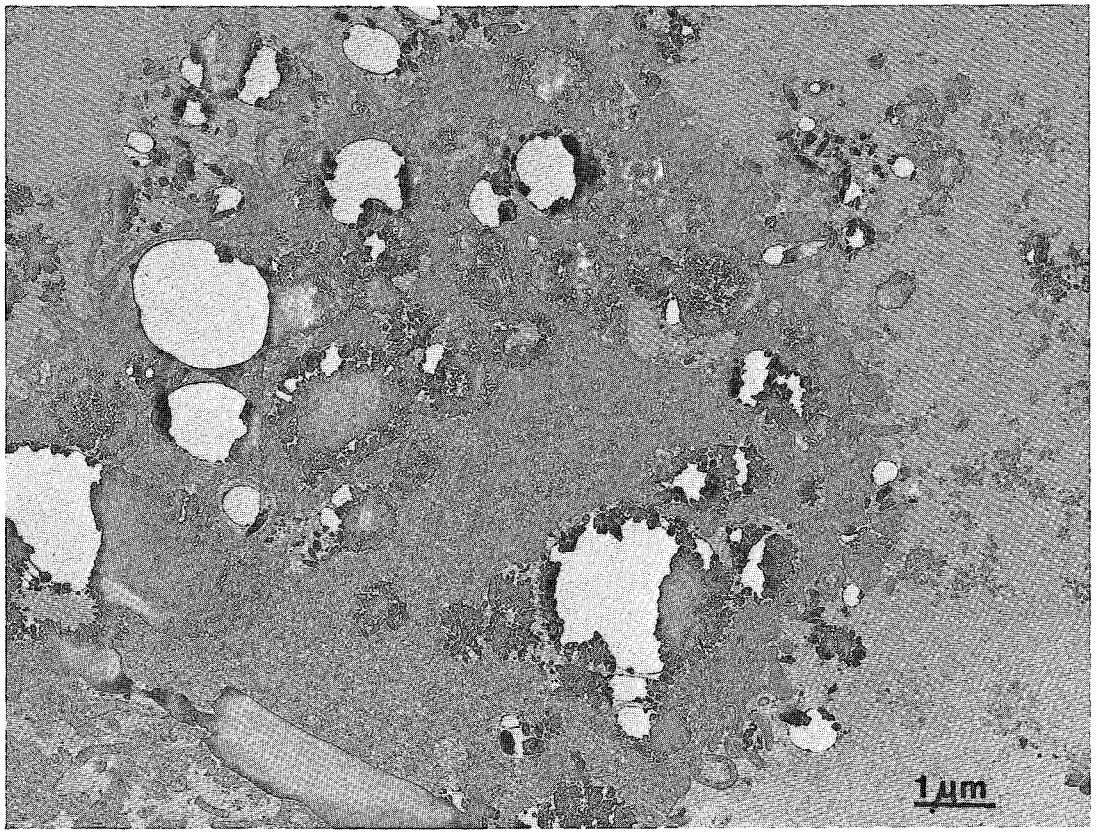

FIG. 5. TEM micrograph of small acicular crystals growing on the edge of silicone vacuoles, themselves included within a macrophage. In a first stage, the crystals form with their longest axis perpendicular to the edge of the vacuoles. Later, the vacuoles are completely filled with crystals. Time elapsed since implantation is unknown.

The comparison of three spectra (Fig. 7) clearly demonstrates the presence of a characteristic band at 950 cm^{-1}, related to zinc cation in the structures of different phosphates. In spectrum 1, the carbonate-hydroxylapatite contains only calcium and no zinc; there is no band at 950 cm^{-1}. In spectrum 2, the parascholzite, which contains zinc and calcium ions, shows a medium band at 950 cm^{-1}; the intensity of this band is stronger in the hopeite spectrum. Infrared absorption spectroscopy has a great potential in detecting the presence of zinc in phosphates and could be an indicator of its relative quantity. The advantages of this method are the small quantity of material required (2 mg), easy sample preparation and rapidity.

Statistical analysis

The Kruskal–Wallis test shows that the occurrence of deposits of mineral matter does not depend on the age of the patients at their first implantation. The Wilcoxon test demonstrates a close relation between the presence of deposits and time elapsed since implantation ($h = 13.83$; critical region $\chi^2_{ic} = 3.84$).

The Chi-square test, with Yate's correction, was used in order to test the relations between the pre-

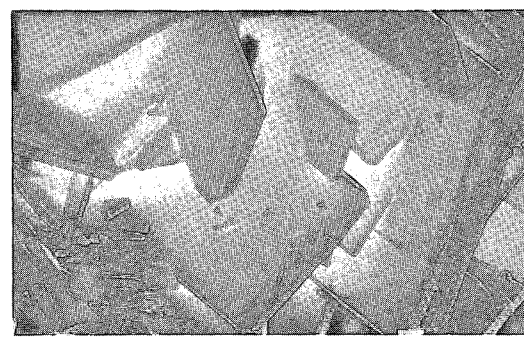

FIG. 6. Thin lamellae of parascholzite in a radiating arrangement. Time elapsed since implantation: 13 years. Scale bar: 10 µm.

TABLE 3. INFRARED FREQUENCIES OF ELEVEN CARBONATE-HYDROXYLAPATITE SAMPLES FROM MAMMARY PROSTHESES

	ν(OH)	δ(OH)	ν(PO_4)				ν(CO_3)			
Sample			1	2	3	4	1	2	3	4
1	3350*	1650	955	–	1030 1090	600, 560	–	860	1400 1445	–
2	3350	1650	955	–	1030 1100	605, 570	–	870	1420 1445	–
3	3340	1650	955	–	1035 1100	610, 570	–	870	1420 1450	–
4	3350	1650	950	–	1030 1095	600, 570	–	850	1410 1450	–
5	3320	1650	950	–	1040 1090	610, 570	–	870	1420 1445	–
6	3360	1650	955	–	1035 1100	605, 570	–	870	1415 1450	–
7	3320	1650	950	–	1030 1090	605, 570	–	865	1410 1450	–
8	3350	1650	960	–	1030 1090	605, 570	–	865	1415 1445	–
9	3350	1650	960	–	1050 1100	610, 570	–	875	1420 1450	–
10	3360	1650	965	–	1040 1100	600, 570	–	875	1420 1450	–
11	3350	1660	960	–	1050 1100	610, 575	–	875	1425 1460	–

* Wavenumber in cm^{-1}

sence of mineral deposits and the following: brand of the prostheses, physical breakdown of the prostheses and Dacron® fixation patches. The occurrence of mineral deposits was closely related to the broken prostheses (χ^2_{ic}: 5.61) and also to the presence of Dacron® fixation patches at the surface of the prostheses (χ^2_{ic}: 29.39) (critical region χ^2_{ic}: 3.84), but no correlation was observed between the occurrence of minerals and the brand of the implants.

Discussion

Whereas carbonate–hydroxylapatite is frequently identified as the major constituent of normally calcified tissues like bones and teeth and is also present in human pathological mineralization as cardiovascular deposits (LeGeros & LeGeros 1984, Roy *et al.* 1983) and breast prostheses (Nicoletis & Wlodarczyk 1983), this is the first report of two zinc phosphates associated with the fibrous reaction of silicone breast implants. Parascholzite is a mineral first described from a Bavarian pegmatite (Sturman *et al.* 1981), and hopeite is a secondary mineral in zinc-bearing ore deposits (Nriagu 1984, Hill & Jones 1976). Both parascholzite and hopeite have not previously been found in humans, either in normal or pathological mineralizations. The unusual presence of zinc as a major constituent of these mineralizations associated with fibrous capsules raises the question of its origin. X-ray-fluorescence analysis of the silicone gel and shell failed to demonstrate the presence of zinc as a constituent of the prosthesis, and

TABLE 4. INFRARED FREQUENCIES OF HOPEITE AND PARASCHOLZITE IN MAMMARY PROSTHESES

	ν(OH)	ν(H_2O)	ν(PO_4)			
Sample	1, 3	2	1	2	3	4
Hopeite	3350,	1650	950	–	1100 1060 1010	630, 580
Parascholzite	3350	1650	960 940	–	1100 1055 1005	660, 635, 590, 550
	3350	1650	960 940	–	1110 1050 1005	650, 600, 590, 555

* Wavenumber in cm^{-1}

no anomalous high-zinc diet on the part of the patients is known. The most plausible source of zinc is the RTV (Room Temperature Vulcanization) glue that is used in the final sealing of the outer envelope (M. Popple, pers. comm.). The possibility of changes in zinc metabolism caused by the surgery could also have some effects (Cornelisse 1986).

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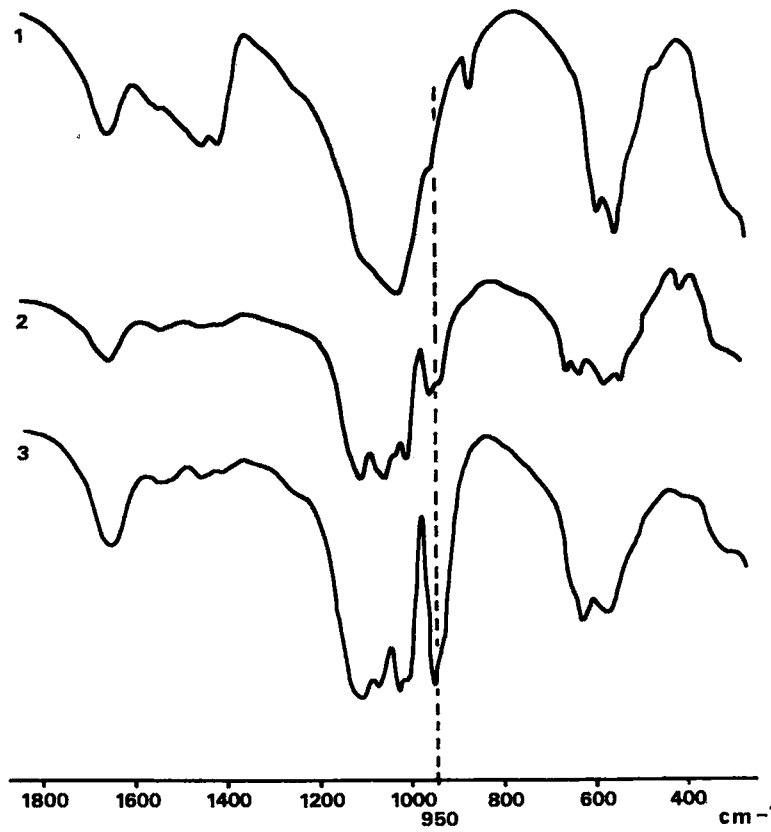

FIG. 7. Infrared absorption spectra of the minerals encountered. 1 carbonate-hydroxylapatite, 2 parascholzite (a band of 950 cm^{-1} is correlated with presence of Zn), 3 hopeite (note that the band at 950 cm^{-1} is more intense).

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