Postmortem Histologic Evaluation of Mandibular Titanium and Maxillary Hydroxyapatite-Coated Implants from 1 Patient

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Postmortem examination of human specimens is an extremely important aspect of evaluating the relative compatibility and long-term success of endosseous implant surfaces. The bone-implant interface of 5 commercially pure titanium screw-type mandibular implants after 85 months of service and 2 hydroxyapatite- (HA) coated maxillary implants after 38 months of service were examined. All implants were stable at the time of the patient's death. The mandibular implants had an average of 65% contact with bone and the maxillary implants had an average of 47% contact. The HA coating had separated from the maxillary implants in some areas and was free within surrounding connective tissue or surrounded by invaginating sulcular epithelium. The arrangement and pattern of bone contact appeared different between HA-coated and titanium implant surfaces. (INT J ORAL MAXILLOFAC IMPLANTS 1999;14:579–586)

Key words: dental implant, Dental Implant Clinical Research Group, endosseous, histology, hydroxyapatite, osseointegration, postmortem, titanium

There is a paucity of postmortem histologic information from long-term, prospective, controlled studies of dental implants. One of the most important questions to be answered is the relative compatibility and long-term success of the most common implant surfaces. The Dental Implant Clinical Research Group (DICRG) is one of the largest randomized scientific clinical studies of implants ever conducted in the United States and is

Reprint requests: Dr Michael D. Rohrer, College of Dentistry, University of Oklahoma Health Sciences Center, 1001 Stanton L. Young Blvd., Oklahoma City, OK 73190. Fax: 405-271-2902. the only study of endosseous dental implants conducted by an agency of the United States government.^{1,2} Postmortem specimens from subjects in this study are becoming available for examination histologically and histomorphometrically.

Since 1991, more than 3,000 implants have been placed and uncovered in more than 800 patients by more than 100 researchers of the DICRG. Because of the nature of the involvement of the subjects and their families in this highly controlled study, many are willing upon their deaths to submit postmortem specimens for examination. Specimens containing both titanium and hydroxyapatite- (HA) coated implants have been evaluated by undecalcified histologic techniques and histomorphometric analysis.³

This particular study involves a patient who had received 5 screw-type titanium implants (Nobel Biocare, Göteborg, Sweden) in the anterior mandible prior to the initiation of the DICRG controlled study. Two maxillary HA-coated cylindric implants (Microvent, Core-Vent, Encino, CA) were placed as part of the study under a secondary protocol. At the time of the patient's death, the mandibular implants had been in place for 85 months and the maxillary implants had been in place for 38 months.

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Patient Description

Social History. The patient was a 77-year-old Caucasian male of Polish descent born in 1919. He used alcohol and tobacco prior to 1973.

Medical History. The patient had suffered from beriberi as a prisoner of war, had bronchial asthma, and was allergic to sulfa.

Dental History. The patient initially presented to the Seattle Veterans Affairs Dental Clinic in 1982 with only the mandibular left premolars remaining. The teeth had been restored with splinted crowns having extracoronal OSO attachments that retained a removable partial denture opposing a complete maxillary denture. The remaining teeth were extracted in February 1989.

After 6 months of healing, 5 commercially pure (cp) 15-mm titanium screw-type implants were placed in the anterior mandible on July 31, 1989. Phase 2 uncovering was accomplished in November 1989, and the final fixed-detachable prosthesis was placed 1 year later, in November 1990. At the 1-month follow-up visit, it was noted that the patient complained of instability of his maxillary denture, which was now functioning against a very stable lower prosthesis.

A 6-month implant prophylaxis was performed in May 1991. The prosthesis was removed, and excellent plaque control and gingival health were noted. The patient was unhappy with his maxillary denture and an occlusal equilibration was performed. One month later, it was noted that the patient's anterior maxillary ridge was becoming fibrous and mobile. His maxillary denture was relined in July 1991, and a new prosthesis fitted to the mouthpiece of his saxophone was placed 3 months later.

The patient was stable for the next year and a half, until May 1993, when the maxillary denture was relined with tissue conditioner. One month later, 2 Microvent implants (3.25 mm \times 10 mm) were placed in the maxillary canine regions. The DICRG study protocol specified 5 implants for the completely edentulous maxilla. Only 2 were placed in this patient because of insufficient bone. Stage 2 surgery was performed on January 21, 1994, and 5mm healing collars were placed. On February 8, it was noted that the healing was progressing slowly and that the healing collars were too short. Straight 4-mm abutments, 4-mm with ball attachments were placed on May 2, 1994, and the relined denture with ball/socket attachments was placed on May 18, 1994. Healing was reported as good at that visit.

The patient next presented in late January of 1995 with the complaint of a loose denture in need

of o-ring replacement. His gingival health was satisfactory, but the denture occlusal surfaces were very worn. Tissue conditioner was placed to correct for the anteroposterior rocking of the denture. It was also noted that the patient's health history had changed. He was then under treatment for hypertension and had had a stroke. His medications at this time included aspirin daily, nifedipine 3 times a day, Beconase nasal inhaler 3 puffs 3 times a day, albuterol 4 puffs twice a day, lasix and potassium every morning, ranitidine every morning for reflux, doxipine at bedtime, tipclopidine twice a day to inhibit platelet aggregation, and Fibercon.

The mandibular implants were evaluated in June 1995. No suppuration was noted, and Periotest values were -6 to -5, indicating clinical integration. The fixed-detachable prosthesis was not mobile and was serviceable.

The DICRG recall for the maxillary implants was performed in August 1995. The Gingival Index was graded at 2 for the mesial of the maxillary right canine implant and for the facial and distal of the maxillary left canine implant, with suppuration present. Periotest values were +2 and +4, respectively. Interprobe measurements were: right maxillary canine implant 3.5 mm mesial, 2.5 mm facial, 3.0 mm distal, 4.5 mm lingual; left maxillary canine implant 7.5 mm mesial, 3.5 mm facial, 7.0 mm distal, 5.0 mm lingual.

Although Periotest values were in the positive range and pocket depths of over 3 mm were present, no mobility of the implants was noted. A culture was taken and the patient was started on tetracycline 250 mg 4 times daily for 14 days. A health history update was significant for recent episodes of pneumonia complicated by the patient's asthma. Culture results were negative, and the patient remained asymptomatic, with a marked decrease in suppuration on September 16. Later that month, the patient suffered another stroke with a residual left leg deficit and was unable to continue treatment.

The patient returned in early December 1995 with an increase in the lingual pocket depth of the left maxillary canine implant to 11 mm, with a corresponding increase in suppuration. The maxillary implants remained non-mobile, and a repair procedure was scheduled for January 1996.

At that appointment a decrease in suppuration was noted. The patient had been on antibiotics for his pneumonia. Probing depths had decreased slightly, to 3.5 mm buccal, 7.0 mm mesial, and 9.0 mm on the palatal and distal. A crestal incision revealed a 3-wall crater defect involving the palatal and extending toward the proximal of the maxil-



Fig 1a Postmortem mandible with 5 cp titanium implants and the fixed-detachable prosthesis.



Fig 1b Postmortem anterior maxilla with 2 HA-coated cylindric implants and ball attachments.

lary left canine implant. The area was thoroughly curetted to remove granulation tissue, and the implant surface was smoothed using a white stone in a high-speed handpiece with copious irrigation. The implant was then detoxified for 3 minutes with a paste of tetracycline. OsteoGraf/N (CeraMed, Denver, CO) was placed in the defect and covered with a Gore-Tex barrier membrane (WL Gore, Flagstaff, AZ). Sutures were removed 5 days later and there was some swelling over the membrane. The patient was again seen on January 23 and showed normal healing.

The patient was next seen on March 1, 1996. At that visit, the area of repair was intact, without erythema or purulence. The patient, however, had declined physically and was noticeably weak. His denture was relined with tissue conditioner so that he could resume wearing the prosthesis. At a 4-day follow-up visit, the gingival tissues appeared somewhat boggy in consistency and less firm than before, with the peri-implant gingiva at the facial aspect described as "loose." The patient was instructed to minimize denture wear.

During this time, the patient's health continued to decline, with several small strokes requiring his admission into a nursing care facility. He returned to the clinic on April 14, 1996, at which time it was noted that there was suppuration around the membrane; the membrane was diagnosed as infected. At membrane removal, the HA repair material was found to be encapsulated in fibrous connective tissue, which was left intact. The implant remained non-mobile. A postoperative prescription for tetracycline (250 mg for 7 days) was provided. One week later, healing was progressing in a slow but normal fashion, with some residual swelling and no purulence. On May 24, the repair side was well healed and alginate impressions were made of both arches in hopes of fabricating new prostheses. The patient was last seen 1 week later. His condition declined rapidly after that, and he died on August 30, 1996. Autopsy specimens were recovered on September 4.

Specimen Preparation

The anterior portions of the mandible and the maxilla were removed at autopsy (Fig 1), placed in 10% neutral buffered formalin and processed without decalcification.^{4,5} The specimens were sectioned to a thickness of 5 mm through the center of the implants-the maxillary specimens in a mesiodistal direction, and the mandibular specimens alternating mesiodistally and buccolingually. Following dehydration, infiltration and embedding were accomplished with a light-curing embedding resin (Technovit 7200 VLC, Kulzer-EXAKT, Norderstedt, Germany). The specimens were cut to a thickness of 150 µm on an EXAKT cutting/grinding system (EXAKT Apparatebau, Norderstedt, Germany), polished to a thickness of 40 µm using the EXAKT microgrinding system, stained with Stevenel's blue and Van Gieson's picro fuchsin, and viewed under conventional light and polarized light microscopy.

Histomorphometric analyses of the light microscopic samples were made to determine the percentage of implant surface in contact with calcified bone, bone marrow, and gingival connective tissue. Photographs were taken with a medical macrolens system to produce \times 1.6 magnification of the implants in the bone. Transparencies were projected to a magnification of \times 75. A digital, programmable curvimeter (K&R Instruments, Orlando, FL) was used to measure the entire

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Fig 2 (*Left*) Mesiodistal section of 2 mandibular cp titanium implants in situ for 85 months. Average bone contact = 68.5%; connective tissue = 14.5%; marrow = 17% (original magnification ×1.6, Stevenel's blue and Van Gieson's picro fuchsin stain).

Fig 3 (Right) Area at cervical of mandibular cp titanium implant in situ for 85 months. Bone contact occurs below level of crestal bone height between third and fourth thread. Epithelium (arrow) contacts implant down to level of bone attachment. Minimal inflammation is present (original magnification ×10, Stevenel's blue and Van Gieson's picro fuchsin stain).

perimeter of the implants. Linear measurements of the connective tissue, bone, and bone marrow contact were made for calculation of the percentage of contact with the implant. Connective tissue was defined as any fibrous tissue in contact with the implant coronal to the most coronal contact point of osseointegrated bone. This included any connective tissue lined by gingival epithelium. Bone contact was defined as intimate interface contact between the bone and the implant surface, with no soft tissue visible between the implant and the bone. Bone marrow was defined as interface contact between soft tissue and the implant surface apical to the most coronal contact point of osseointegrated bone.

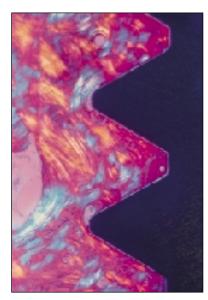
Results

Light Microscopy. Low-power examination showed that the mandibular titanium implants were well integrated, with some crestal loss of bone, but with generally satisfactory height of bone on the implants. The buccolingual sections showed a relatively dense and continuous integration of bone to implant surface where the implants were close to the cortical bone of the buccal or lingual plates. The mesiodistal sections showed more bone marrow contact in the predominantly cancellous bone area (Fig 2). A higher-power view of the coronal area demonstrated some crestal bone loss in 3 of the implants; that is, bone contact with the implant more apical than the height of the crestal bone surrounding the implant. This generally was at the third thread. Sulcus epithelium was in contact with the implant to the point of bone contact (Fig 3). Very slight inflammation was present in the connective tissue. The bone bordering this "ditch" area exhibited a surface layer of osteoid tissue and osteoblasts, indicating active osteogenesis. The bone surrounding the apical portion of the implants was very dense. The bone in the apical vents was less dense but showed a high degree of bone contact.

Polarization of the stained sections showed that the bone contacting the implants was mature and remodeled Haversian bone. Within the threads, the remodeled lamellar patterns consisted of much smaller osteons as opposed to the general, larger lamellar patterns of the bone farther from the implant (Fig 4a). The trabeculae in the cancellous bone area were generally oriented around the implant in a supporting, strut-like buttressing pattern (Fig 4b). Polarized light microscopy of the bone in this area also emphasized the remodeling pattern of the bone to conform to the architecture of the threads (Fig 4c).

The amount of bone contact with the maxillary HA-coated implants was clearly less than with the mandibular implants; however, where there was contact it tended to be more continuous than in the titanium implants. Low-power mesiodistal views showed deep cratering of the bone around the implant from the maxillary right canine implant area and better bone contact with the implant in the maxillary left canine implant area. Particles of hydroxyapatite that were placed around the implant in an attempt at gaining greater bone support were also obvious. Higherpower views of the crestal area revealed that

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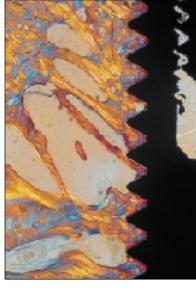


Fig 4a Polarized light view of area of bone within the threads of mandibular cp titanium implant in situ for 85 months. Polarization emphasizes the smaller osteons in the thread area compared to the generally larger lamellar patterns farther from the implant (original magnification ×25, Stevenel's blue and Van Gieson's picro fuchsin stain).

Fig 4b Polarized light view of cancellous bone surrounding mandibular cp titanium implant in situ for 85 months. Supporting trabeculae are arranged in a strut-like buttressing pattern (original magnification $\times 6.25$, Stevenel's blue and Van Gieson's picro fuchsin stain).

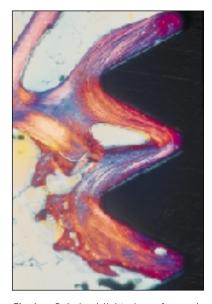


Fig 4c Polarized light view of cancellous bone surrounding mandibular cp titanium implant in situ for 85 months. The polarization emphasizes the remodeling pattern of the bone to conform to the architecture of the threads (original magnification ×25, Stevenel's blue and Van Gieson's picro fuchsin stain).

epithelium from the gingiva followed the implant surface to well below the level of the crestal bone. Also, separation of the HA coating from the titanium surface in some areas was evident (Fig 5). Not all areas of the HA-coated implant not in intimate contact with the bone show the HA separation, but the epithelium had migrated along the entire HA surface to the point of first bone contact (Fig 6).

Where bone was in tight apposition with the HA-coated implant, especially in the apical areas and within the apical vents, the bone was dense, solid, and mature. The character of this bone in contact with the HA was almost a continuous band of calcified bone, with 90% of the bone being calcified and 10% marrow (Fig 7). The bone had remodeled in the areas of implant contact to conform to the surface configuration of the implant (Fig 8). In some areas where new bone formed around the implant, loose pieces of HA coating were incorporated into the bone. Obviously the HA had separated from the implant in vivo, because the pieces of HA were surrounded by invaginating epithelium, and in some areas the epithelium was between the titanium surface and the separated HA coating (Fig 9).

Histomorphometric Analysis. Histomorphometric analysis of the bone and soft tissue contact of the implants revealed 18% more contact with bone on the mandibular implants than the maxillary implants, with 47% of the maxillary implants with intimate bone contact and 65.4% of the mandibular implants with bone contact. Of the 2 maxillary HA-coated implants, there was much less bone contact on the right canine implant (38%) than on the left (56%). The bone contact on the mandibular implants was very uniform, ranging from a high of 72% to a low of 62%. A conspicuous difference between the HA-coated and cp titanium implants was seen in the amount of marrow contact. The maxillary HA-coated implants had an average of 5% marrow, and the mandibular cp titanium implants had an average of 19.4%. This is a measure of the continuity of the bone contact within the osseointegrated areas of the implants and indicates a more uninterrupted solid bone contact with the HA coating.

The measurement for connective tissue contact is the measure of the amount of implant that is "out of the bone" and could actually represent gingival connective tissue, connective tissue lined by epithelium, or a portion of the implant totally exposed to

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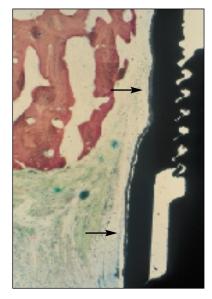


Fig 5 Mesiodistal section of HA-coated maxillary right canine implant in situ for 38 months. Gingival epithelium *(arrows)* is in contact with the HA well apical to the level of bone. Separation of HA coating from the implant is seen (original magnification × 6.25, Stevenel's blue and Van Gieson's picro fuchsin stain).

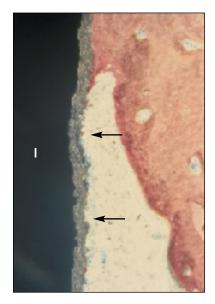


Fig 6 Hydroxyapatite-coated maxillary right canine implant in situ for 38 months. The HA coating is tightly adherent to implant (I). Gingival epithelium has migrated all the way to the point of first bone contact (*arrows*). No inflammation is present in the connective tissue (original magnification ×25, Stevenel's blue and Van Gieson's picro fuchsin stain).

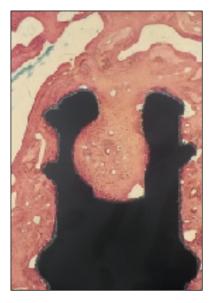
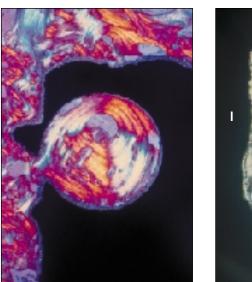


Fig 7 Apical area of HA-coated maxillary left canine implant in situ for 38 months. Tight contact of dense, solid, mature bone can be seen in almost continuous contact with the HA-coated implant (original magnification ×6.25, Stevenel's blue and Van Gieson's picro fuchsin stain).



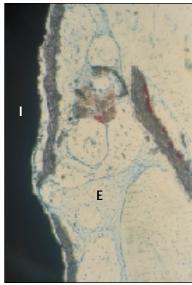


Fig 8 *(Left)* Polarized light view of apical vent area of HA-coated maxillary left canine implant in situ for 38 months. The polarization emphasizes the remodeling of the bone in contact with the implant to conform to the configuration of the implant surface. Note the difference in the lamellar pattern within the vent and the pattern of the bone surrounding the implant (original magnification ×10, Stevenel's blue and Van Gieson's picro fuchsin stain).

Fig 9 (*Right*) Hydroxyapatite-coated maxillary right canine implant in situ for 38 months. Implant (I) and separated HA coating, which has been surrounded by invaginating sulcular epithelium (E), demonstrate that the HA coating had separated in situ (original magnification ×25, Stevenel's blue and Van Gieson's picro fuchsin stain).

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Table 1 Bone and Soft Tissue Contact with Implants				
		Amount of contact (%)		
Location/implant	Bone	Connective tissue	Marrow	
Right maxilla/HA	38	58	4	
Left maxilla/HA	56	38	6	
Left mandible/titanium	63	15	22	
Left central mandible/titanium	72	12	16	
Central mandible/titanium	65	17	18	
Right central mandible/titanium	65	16	19	
Right mandible/titanium	62	16	22	
Average, maxilla	47	48	5	
Average, mandible	65.4	15.2	19.4	

the oral cavity. In regards to this parameter, the maxillary HA-coated implants were much less integrated, with an average of 48% not in bone, while the mandibular cp titanium implants showed an average of 15.2% coronal to the first bone contact. At least 2 sections of each implant were measured to arrive at the measurements for the bone and soft tissue contact. The measurements for all categories on all 7 implants can be seen in Table 1.

Discussion

This study of postmortem histologic features involving maxillary and mandibular implants with HA coatings and titanium surfaces is a valuable correlation between clinical parameters of implant success and actual implant osseointegration. Only a few studies of in situ implants in humans have been reported.^{3,6–9} Although in this study the clinical parameters of peri-implant inflammation and pocket depth suggested that the maxillary HAcoated implants should have been less than satisfactory, they were acceptable to the patient. Regardless of the inflammation and loss of attachment, the stability and serviceability of the implants benefited the patient.

The difference in the pattern of bone contact on the different types and locations of implants was interesting. Clinicians generally consider the bone of the mandible to be of higher quality than the maxilla and would assume that the quality and quantity of the osseointegration there would be greater.^{10,11} Although the percentage of the bone contact was higher on the mandibular cp titanium implants, bone contact was more uniform and solid on the maxillary HA-coated implants. As can be seen in Figs 4b and 7, the bone contact patterns in the maxilla and mandible—and therefore in HA-coated and titanium implants—were very different. It is obvious that the bone was much higher coronally on the mandibular cp titanium implants than on the maxillary HA-coated implants. The average of 15.2% connective tissue contact on the mandibular cp titanium implants and 48% connective tissue contact on the maxillary HA-coated implants illustrates this. A major difference between the 2 areas and types of implant surfaces in this study is that in the area of bone contact, there is almost solid bone surrounding the maxillary HA-coated implants, with only 5% marrow contact. There is much more marrow in the mandibular cp titanium (19.4%), indicating more cancellous bone in tight contact with the implant.

The surface of the maxillary HA-coated implants that was covered by connective tissue, which is coronal to any bone contact, showed a reasonably large amount of loss of HA from the surface of the implants. A feasible explanation for the presence of HA in the soft tissue adjacent to the maxillary left implant was the curettage and smoothing of the implant surface with a rotary white stone at the time of the surgical approach to the 3-wall defect. Separation of HA from the maxillary right implant can be seen in Fig 5, which is difficult to determine as pre- or postmortem.

The use of polarized light in viewing the specimen sections emphasizes the remodeling pattern of the mature bone. As could be seen in Figs 4 and 8, the pattern of bone changed to accommodate the stresses placed upon it by the introduction of the implant. The functional forces transmitted through the implant to the bone seem to have influenced the remodeling pattern of the collagen structure of the bone. Bone in contact with the implant that is denser than the surrounding cancellous bone has been observed in other investigations.^{3,12}

In this study, the surfaces of the implants, whether cp titanium or HA, were covered by gingival epithelium coronal to the area of first bone contact (Figs 3 and 5). This is similar to what was found in a postmortem study of 12 implants in 4 quadrants.⁶ However, in another postmortem investigation involving a patient from the DICRG prospective study, the peri-implant mucosa showed clinical and histologic resemblance to the gingiva around natural teeth. In that study, a thin, nonkeratinized epithelium lacking rete ridges and looking like sulcular epithelium was present surrounding the necks of the implants. Coronal to the bone contact and between the bone and epithelium, connective tissue was tightly adherent to the implants, with bundles of collagen organized in the pattern of cervical gingival connective tissue.³

Noticeable differences were seen in this study between the maxillary HA-coated implants and the mandibular cp titanium implants. However, because all of the implants were not placed according to the randomized protocol of the DICRG, it is difficult to discern differences that may be the result of location and function as opposed to surface coating. Additional postmortem examinations of patients who have been treated under prospective, controlled implant studies will help answer the question of the reaction of bone to the placement and long-term function of implants with various surfaces presented to the bone of the human jaws.

Conclusion

A postmortem histologic examination of the boneimplant interface of 5 cp titanium screw-type mandibular implants was carried out after 85 months of service and of 2 hydroxyapatite (HA) coated maxillary implants after 38 months of service. All implants were stable and satisfactory to the patient at the time of his death. The mandibular implants had an average of 65% contact with bone, and the maxillary implants had an average of 47% contact. The condition of the mandibular implants that had been in place for more than 7 years was excellent, with little inflammation around the implants and more than 80% of the length of the implants within bone. The maxillary HA-coated implants were stable, even though they had slightly less than 50% bone contact and had experienced peri-implantitis. They were considered stable by the clinicians and satisfactory by the patient. The HA coating appeared separated from the implants in some areas and in the area of the left maxillary implant it was both free within surrounding connective tissue and surrounded by invaginating sulcular epithelium. The presence of these HA fragments was most likely caused by instrumentation of the implant surface during surgical treatment of a bone defect in the area. The pattern and arrangement of bone contact was different between the maxillary HA-coated and the mandibular cp titanium implants.

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