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Evaluation of Vascularization of Hydroxyapatite Ocular Implants by ^{99m}Tc-MDP Bone Scan: Preliminary Study

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= **국문초록** =

^{99m}Tc-MDP 골주사를 이용한 Hydroxyapatite 안구보충물의 혈관신생에 관한 예비연구

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목 적 : 안구제거술 후에 삽입한 hydroxyapatite 안구보충물내로 혈관신생이 완전하게 일어나는 시기를 알아보기 위함이다.

방 법 : 안구제거술을 받은 43예의 환자(남자 33예, 여자 10예, 14-56세)에게 대부분 변경되지 않은 방법으로 hydroxyapatite 안구보충물을 삽입한 후 10-23주 사이에 다양한 간격(10-12주 2예, 13-16주 18예, 17-20주 20예, 21-23주 3예)을 두고 ^{99m}Tc-MDP 골주사를 시행하여 보충물내로의 혈관신생 정도를 전향적으로 측정하였다. 정면 및 측면촬영의 정적영상에서 안구보충물의 방사능섭취가 비교(nasal bridge)의 방사능섭취보다 약할 경우를 grade 1, 같을 경을 grade 2, 강할 경우를 grade 3로 나누었으며 grade 2와 3을 혈관신생이 완전하다고 정의 하였다. 또한 43예 모두에서 방사능섭취 정도와 관계없이 안구보충물 삽입후 평균 21주 되는 시기에 안구보충물에 구멍을 내어 이 구멍으로부터의 출혈여부를 확인한 후 운동성나사(motility peg)를 끼워 의안(prosthesis)과 연결하였다. 43예중 7예에서는 ^{99m}Tc-MDP 골주사와 조영제주입후의 자기공명영상(Gd-DTPA T_1-weighted images)을 같은 날짜에 시행하여 각각의 예에서 방사능섭취 정도와 조영제증강 정도를 비교하였다.

결 과 : 안구보충물내로 완전하게 혈관신생이 일어났던 grade 2와 3의 비율은 안구보충물 삽입후 10-12주에서는 0%, 13-16주 33%, 17-20주 50%, 21-23주 67%로써 시간경과에 따라 점차 증가하였다. 골주사소견에 관계없이 안구보충물 삽입후 평균 21주되는 시기에 보충물 앞쪽에 구멍을 내었을 때 43예 모두에서 완전한 혈관신생을 의미하는 출혈을 볼 수 있었다. ^{99m}Tc-MDP 골주사와 조영제주입후의 자기공명영상을 둘 다 시행한 7예 각각에서 방사능섭취의 정도와 조영제증강의 정도가 거의 일치하였다.

결 론 : 본 예비연구의 결과로써 hydroxyapatite 안구보충물 삽입후 21주째에 ^{99m}Tc-MDP 골주사를 시행하는 것이 좋을 것으로 생각되며, hydroxyapatite 안구보충물내로의 완전한 혈관신생 여부를 보는 데에는 ^{99m}Tc-MDP 골주사가 조영제주입후의 자기공명영상보다 더 경제적이라고 할 수 있겠다.

Key Words : Ocular implant, Bone scan, Vascularization

INTRODUCTION

Ocular implants are used to replace the volume of the orbit following enucleation as well as to allow the artificial eye to move in conjunction with the normal eye when the artificial eye is coupled to the implant. One of the difficulties with the previous methods of orbital implantation after enucleation is the poor motility of the implant/prosthesis complex. This is a result of a lack of transfer of motion from the nonintegrated implant to the prosthesis. The hydroxyapatite implant is directly integrated or attatched by a peg to the prosthesis for motility purposes. This implant appears to be well tolerated and has been shown to provide improved prosthesis motility with very few complication. It must be vascularized to support epithelialization of a hole drilled in its anterior face for insertion of a motility peg[1-6].

Radionuclide scanning with Tc-99m methylene diphosphonate(^{99m}Tc-MDP) has been used to assess implant vascular ingrowth because radiophosphate deposition within the hydroxyapatite sphere parallels vascularization[1]. To evaluate the time course for vascularization, we performed ^{99m}Tc-MDP bone scan prosepectively at various intervals after implantation, because if the rate of vascularization can be increased, the motility hole can be drilled earlier, resulting in more rapid cosmetic rehabilitation of the patient[6].

MATERIALS AND METHODS

Forty-three patients(33 males and 10 females, range of age : 14-56 years, mean 34 years) undergoing standard, uncomplicated enucleation (9 patients) or evisceration(34 patients) received primary coralline hydroxyapatite ocular implants with unmodified technique principally. At various intervals from 10 to 23 weeks after implantation, graft vascularization was evaluated by using ^{99m}Tc-MDP bone scan prospectively. After intravenous injection of 20 mCi of ^{99m}Tc-MDP, dynamic images were obtained at 1 frame per second for 60 seconds by computer acquisition, immediately after injection. A static blood pool images was then obtained. Static images were performed at 2-2.5 hours in the anterior and both lateral projections using a large-field-of view camera(Toshiba digital camera, GCA-601E) with low-energy all-purpose collimator at 140 keV and 20% window. Two patients were studied at 10-12 weeks, 18 patients at 13 to 16 weeks, 20 patients at 17-20 weeks, and 3 patients at 21 to 23 weeks after implantation. Activity was assessed for relative intensity on planar images and scored as less than(grade 1), equal to(grade 2), or grater than(grade 3) the nasal bridge activity, and grade 2 and 3 were regarded as complete vascularization of the implants. A central 4 mm hole for the motility peg was drilled radially into the hydroxyapatitie sphere in all patients irrespective of activity on the ^{9m}Tc-MDP scan at, on the average, 21 weeks(3 patients at 15-17 weeks, 24 patients at 20 weeks, 11 patients at 21-24 weeks, 4 patients at 25-28 weeks, and 1 patient at 31 week) after implantation and whether bleeding or not from the drilled "well"(suggesting complete fibrovascular penetration) was observed. In 7 out of 43 patients MRI was performed before and after 0.1 mmol/kg Gd-DTPA administration on the same day of ^{99m}Tc-MDP scan and pre- and postcontrast T1-weighted images were compared for evaluation of the degree of enhancement, which was graded as mild(grade 1), moderate(grade 2), and marked(grade 3) enhancement. In each patient the degrees of vascularization on these two examinations were compared.

RESULTS

Increased activity of grade 2 and 3 on ^{99m}Tc-MDP scan was seen in none(0%) at 10-12 weeks, in 6 of 18 patients(33%) at 13-16 weeks, in 10 of 20 patients(50%) at 17-20 weeks, and in 2 of 3 patients(67%) at 21-23 weeks after implantation(Table 1).

The earliest one was seen at 14 weeks after implantation(Fig. 1). Bleeding from the drilled "well" was seen in all patients when a central hole for the motility peg was drilled irrespective of activity on ^{99m}Tc-MDP scan at, on the average, 21 weeks after implantation. In 7 out of 43 patients studied with both ^{99m}Tc-MDP scan and MRI, the degrees of vascularization were very similar on the two examinations in each patient(Fig. 2, 3).

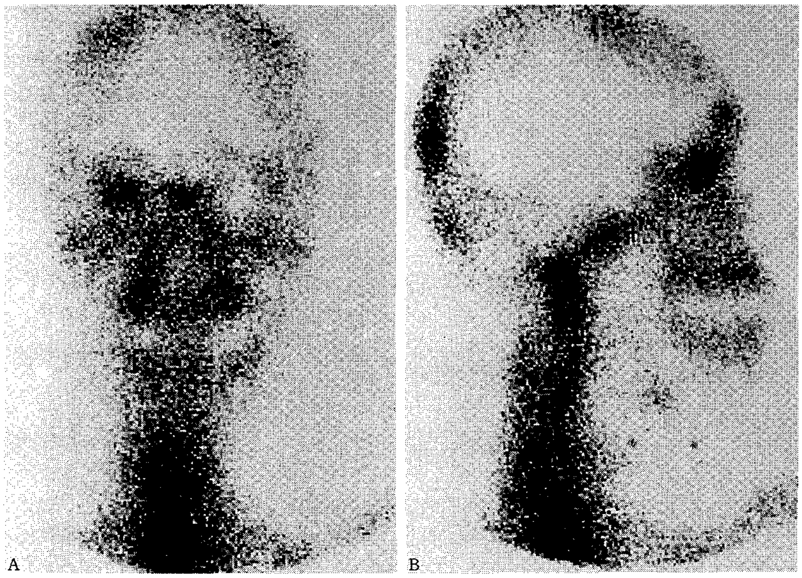

Fig. 1. The earliest vascularization of the hydroxyapatie ocular implant. Anterior(a) and right lateral(b) ^{99m}Tc-MDP bone scan images of the head of a patient 14 weeks after implantation reveal increased uptake in the right orbit similar to that of nasal bridge. Bleeding was seen when drilling the central hole in the implant one week later.

Table 1. Vascularization of Hydroxyapatite Implant by ^{99m}Tc-MDP Scan

Time interal between implantation & Scan(weeks)	No. of Cases	Increased Uptake		Total
		Grade 2 or 3	Grade 1	
10 - 12 W	2	0	0	0
- 16 W	18	6(33%)	3(17%)	9
- 20 W	20	10(50%)	2(10%)	12
- 23 W	3	6(67%)	1(33%)	3
Total	43	18(42%)	6(14%)	24

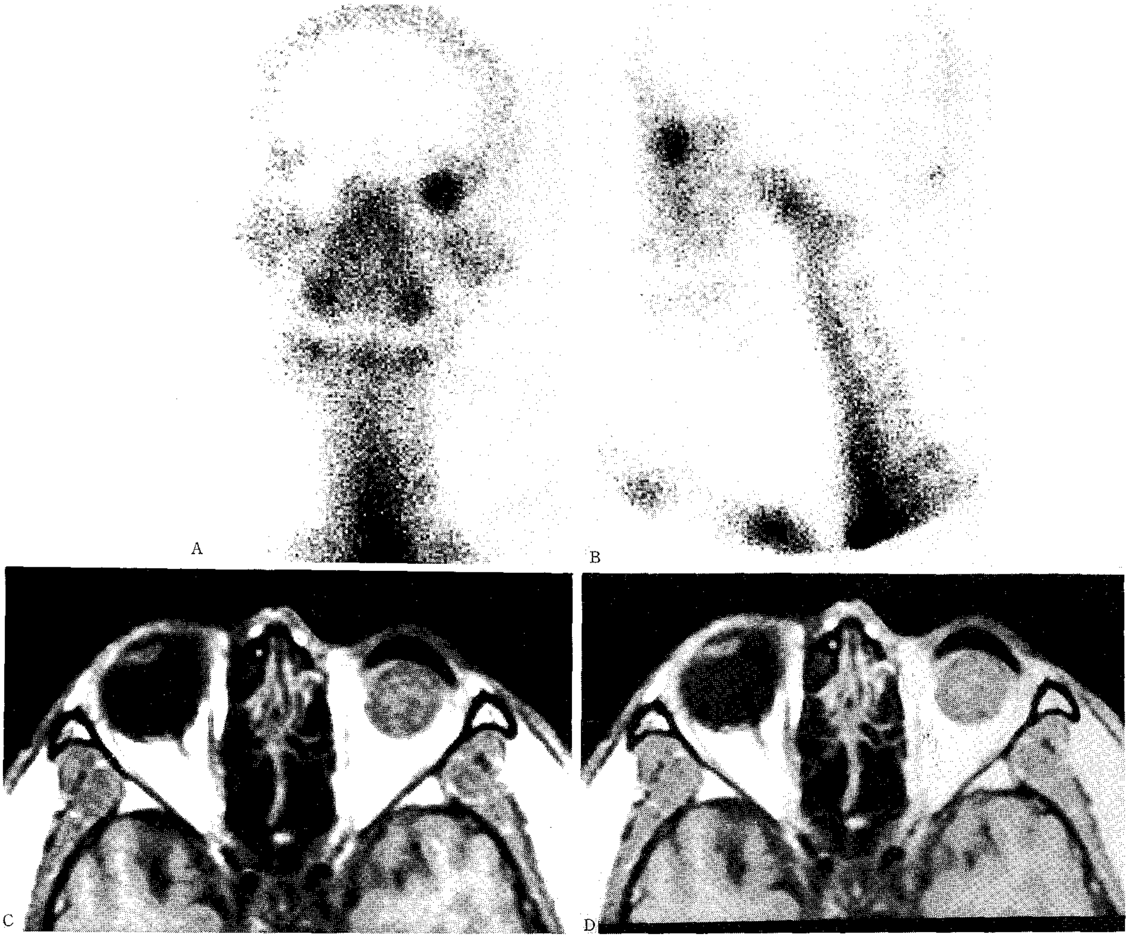

Fig. 2. Anterior(a) and left lateral(b) ^{99m}Tc-MDP bone scan images of the head of a patient 20 weeks after implantation show increased uptake in the left orbit greater than that of nasal bridge. Pre-(c) and postcontrast(d) T1-weighted images of the orbit reveal marked enhancement in the left ocular implant.

DISCUSSION

Porous hydroxyapatite is a material derived from the skeletal stucture of specific marine corals composed primarily of calcium phosphate, a normal constituent of bone, with a regular system of interconnection pores similar to cancellous bone, which can act as a passive latticework for fibrovascular ingrowth when the material is implanted into human tissue. Since initial introduction in 1985(and FDA approval in 1989), porous hydroxyapatite implants have been used for maxillofacial onlay grafting, alveolar ridge augmentation, cranial reconstruction over dura, middle ear reconstruction, laryngeal framework support, repair of orbital floor fractures, and post-traumatic long bone grafts, because it has been shown to be nontoxic, biocompatible, and nonallergenic in humans[7-10]. Hydroxyapatite spheres have been used clinically as orbital implants since 1989[2, 5].

Coralline hydroxyapatite ocular implants are spheres covered with sclera to allow vessels from

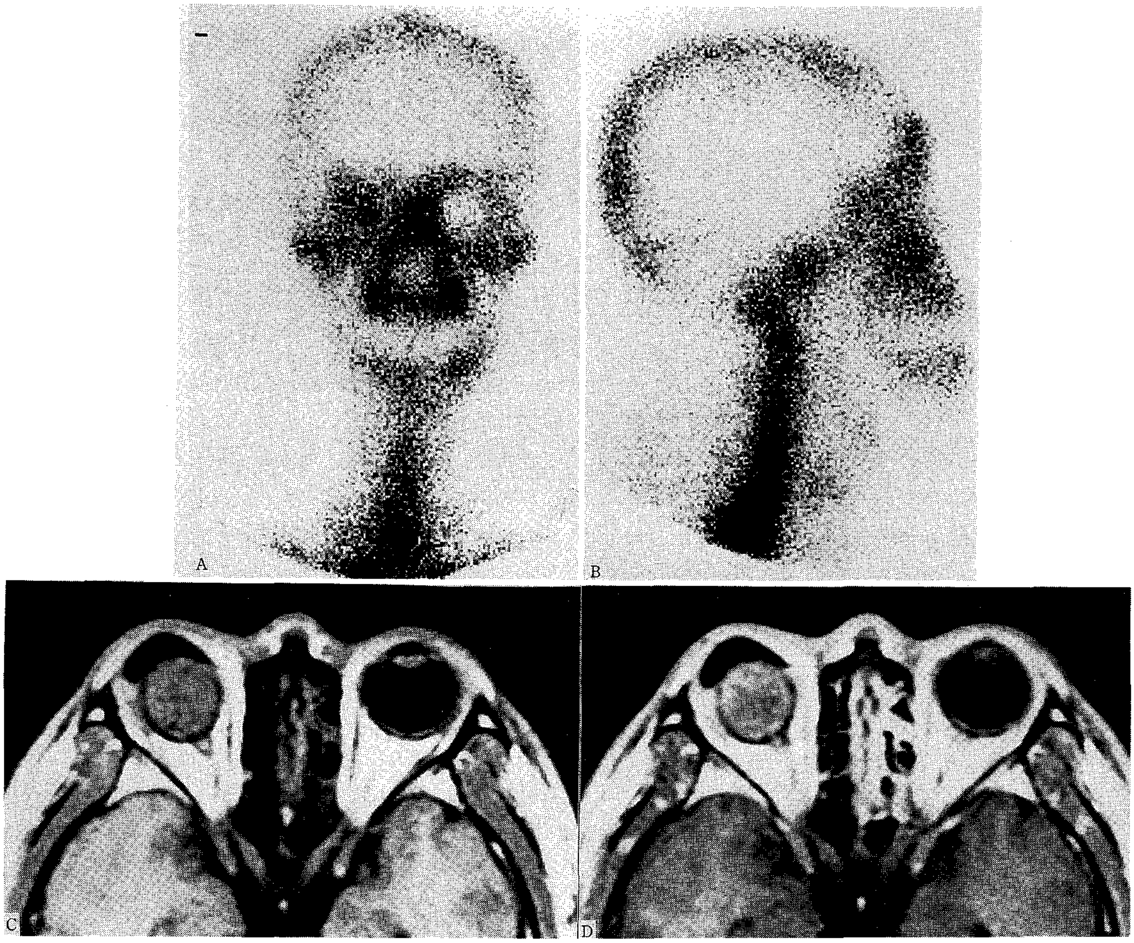

Fig. 3. Increased uptake similar to that of nasal bridge is seen in the right orbit on anterior(a) and right lateral(b) ^{99m}Tc-MDP bone scan images of the head of a patient 20 weeks after implantation. Pre-(c) and postcontrast(d) T1-weighted images of the orbit show moderate enhancement in the right ocular implant.

their anterior ciliary arteries to grow into th ball. Once the sphere is implanted into the orbit, there is growth of fibrovascular tissue into the pores of the implant in a creeping centripetal fashion from the periphery toward the centre and it is most extensive near the scleral defects for attachment of the extraocular muscles. This fibrovascular ingrowth is necessary before exposure of the implant for coupling to the artificial eye. The coupling is achieved by means of a motility peg, which is placed into a hole drilled into the implant and then coupled to the artificial eye by a ball-and-socket type joint with transfer of the increased motility of the implant to the posthesis(Fig. 4). This hole should not be drilled while the sphere is avascular because if the hole is drilled into a nonvascularized hydroxyapatite sphere epithelialization will be delayed and infection could result, since the peg and nonvascularized portion of the implant are essentially foreign bodies in contact with the external environment[1-4]. Vascularization of the implant is

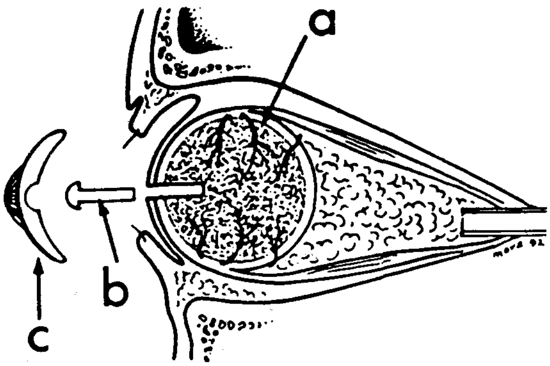

Fig. 4. Schemetic diagram of a vascularized hydroxyapatite ocular implant(a=ocular implant; b=coupling peg; c=eye prosthesiss)(cited from reference 11).

a prerequisite for epithelialization of the drilled "well"(hole) that houses the motility peg. Epithelialization is necessary to prevent infection of the orbit and extrusion of the hydroxyapatite sphere. If the surgeon sees bleeding when drilling the central "well", he is assured that epithelialization will occur within 4-6 weeks[5]. But the time for the sphere to vascularize before safely drilling the transconjunctival hole for the motility peg is controversial[1, 4, 5]. In the recent reports, histopathologic study of an orbital hydroxyapatite implant that was removed 4 weeks after implantation showed infiltration by fibrovascular tissue within the pores of the sphere[3, 4]. But a minimum of 6 months has been recommended, with a ^{99m}Tc-MDP scan to confirm vascularization before drilling[1].

^{99m}Tc-MDP scintigraphy is a noninvasive method of evaluating the successful integration into the normal orbital tissues and therefore the optimal time for coupling with the artificial eye to afford motility. ^{99m}Tc-MDP has been observed to localize in incorporated implants implying delivery by vascular ingrowth. The mechanism of localization has not yet been determined. Activity in the hydroxyapatite spheres is likely due to adsorption of the ^{99m}Tc-MDP to the hydroxyapatite matrix. Regardless of mechanism of ^{99m}Tc-MDP localization, activity within the implant indicates ingrowth of blood supply. Initial assessments of vascularization have emphasized intensity of ^{99m}Tc-MDP deposition within the implant[5, 6].

Perry[1] has defined a grading system for characterizing the uptake of radiotracer in hydroxyapatite ocular implants. Uptake of 4+ is uptake in the implant greater than that in the midfacial bones, 3+ is equal to the midfacial bone, 2+ is midway between the midfacial bones and the normal orbit, while 1+ is greater than the normal orbit but not quite 2+. Uptake of 2+ or better in the implant demonstrated the successful ingrowth of fibrovascular tissue into the implant. Numerow et al[11]. assessed the activity for uniformity on planar and single photon emission tomographic(SPECT) images in 15 patients studied 6 months following hydroxyapatite orbital implantation and activity was scored as less than, equal to, or greater than the nasal bridge activity. Their results showed that complete vascularization was best defined by planar imaging rather than SPECT. They proposed that uniformity of activity was probably more significant while the relative intensity of implant activity might be an important feature. Calculating with the letter, the rate of complete vascularization was 67%(10/15) at 6 months after implantation in their study.

Ferrone et al[6]. studied the rate of vascularization in 12 hydroxyapatite implants after enucleation surgery using a modified technique by drilling additional access holes to encourage more rapid host tissue ingrowth. They monitored vascularization with both static and dynamic bone scans performed at various intervals(from 8 weeks to 16 weeks) after surgery. Where vascular ingrowth was incomplete, the implant showed only an enhanced rim of activity with little or no central activity. When vascularization was complete, intense activity was measured throughout the entire implant. Their study showed that with a simple modification of the coral implant to allow more rapid tissue ingrowth, vascularization could be completed much earlier, at about 10 weeks after surgery. Using unmodified technique, Perry[1] and Dutton [5] found vascularization to be relatively slow, usually requiring at least 6 months and, in some cases, as long as 10 months. Drilling of a hole for the motility peg, which allows integration to the prosthesis, is delayed until this point, since vascularization of the hole walls is necessary to allow lining by conjunctiva.

In our prosepective study, the rate of complete vascularization was increased with time from 13 weeks to 23 weeks after implantation(33% to 67%). When, irrespective of activity on ^{99m}Tc-MDP scan, a central hole for the motility peg was drilled at about 21 weeks after implantation on the average in each patient, bleeding from the drilled "well" was observed in all of them. From these results, we speculated that the 21th week after implantation, which was somewhat eariler than that of previous report[1], might be appropriate time for pre-drilling ^{99m}Tc-MDP scan for evaluation of vascularization of the hydroxyapatite implants and that a central hole could be drilled at this time if the activity would be grade 2 or 3. Recent reports[12, 13] of Gd-DTPA-enhanced MRI of hydroxyapatite orbital implants has described both uniform and nonhomogenous peripheral patterns of enhancement in the vascularized implants. After intravenous administration of Gd-DTPA on T1-weighted images, variable hyperintense signal areas in the hydroxyapatite implant suggested the presence of fibrovascular ingrowth. De Potter et al[12]. reported that there was no definite correlation between the extent of hydroxyapatite implant enhacement and the time interval that elapsed after implantation in 15 patients examined from 5 to 13 months after enucleation. They thought that this observation might reflect individual variations in angiogenesis. The presence of enhnacement rather than the characteristics of this enhancement was their guide for drilling. They reported that contrast-enhanced MRI provided a reliable determination of implant vascularization and greater anatomic detail than ^{99m}Tc-MDP scan because of its three-dimensional capability and its highest resolution. But they did not describe either an adequate time for MRI examination or the rate of vascularization following implantation. In our limited experience of 7 patients using both ^{99m}Tc-MDP scan and contrast-enhanced MRI, we found that the degree of vascularization of hydroxyapatite ocular implants appeared very similar in these two examinations, i.e., the grades of both activity and enhancement were almost same in each patient.

In conclusion, vascularization could be completed at about 21 weeks after implantation, so this time seems to be appropriate for pre-drilling ^{99m}Tc-MDP scan. ^{99m}Tc-MDP bone scan seems to be more cost-effective than contrast-enhanced MRI for evaluation of vascularization of the hydroxyapatite ocular implants.

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