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Review of human and animal  
studies on maxillary sinus  
grafting for implant  
placement

조선대학교 대학원

치의공학과

박 열 수



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임프란트 식립을 위한 상악동 점막 거상술의 문헌고찰 :  
사람과 동물 연구

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이 논문을 치의학 박사학위신청 논문으로 제출함

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# 박열수의 박사학위논문을 인준함

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## 국문초록

### 임프란트 식립을 위한 상악동 점막 거상술의 문헌고찰 : 사람과 동물 연구

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본 연구의 목적은 상악동 점막 거상술에 대한 동물과 사람에 대한 연구의 차이와 성공률에 대한 비교 및 향후 연구의 전망에 대해 논하고자 한다.

1997년부터 2006년까지 임프란트 식립을 위해 시행된 상악동저 점막 거상술에 대해 보고된 문헌을 Medline을 통해 검색하였다. 검색시 사용한 key word는 sinus augmentation, sinus graft, sinus lift, sinus elevation, animal이었다.

상악동 점막 거상술에 관한 동물실험은 주로 양과 미니돼지가 실험대상 이었으며, 골-임프란트 접촉률을 평가하는 논문이 대부분이었고, 사람을 대상으로 하는 논문은 주로 임상적 성공률(survival rate)에 관한 논문이 주를 이루었다.

상악동 점막 거상술의 동물실험시 임프란트의 식립 시기, 희생 시기, 조직학적 평가 기준 등에 관한 근거를 바탕으로 시행하여야 할 것으로 보이며 양, 돼지, 개 등을 이용한 상악동 점막 거상술의 실험은 새로운 임프란트나 골대체제 등에 관한 연구에 있어 임상실험 전에 중요한 과정으로 여겨진다.



# I . Introduction

Methods to overcome insufficient bone due to poor bone quality, the pneumatization of a maxillary sinus and other anatomical limitations of implant placement in the maxillary molar area include the augmentation of residual alveolar bone using bone grafting with onlay grafts<sup>1</sup> or veneer grafting and bone grafting methods involving a Le Fort I osteotomy.<sup>2</sup> Of these, the maxillary sinus lift is a simple procedure, has fewer side effects than other techniques, and can be widely applied. After it was introduced by Tatum<sup>3</sup> and Bonye,<sup>4</sup> Tatum<sup>3</sup> reported a procedure involving implant placement and simultaneous maxillary sinus bone grafting using a lateral wall approach. Despite numerous subsequent studies that examined various clinical techniques and bone graft materials, it is still recognized as the most reliable method. Both animal studies and clinical studies on patients have examined the maxillary sinus lifting. In this study, the success rate and the differences between animal and human studies from the literature study were compared and then the future perspectives of studies on the maxillary sinus lifting were discussed.

## II. Methods

Papers published between 1997 and 2006 on the maxillary sinus grafting for implant placement were surveyed through the Medline. The keywords used for this survey were sinus augmentation, sinus graft, sinus lift, sinus elevation, and animal.

### III. Results

In the literature study, 38 papers dealt with animal experiments on maxillary sinus floor lifting were found. Among the animal studies, sheep and minipig were mostly used as the experimental animal, in terms of the evaluation of the bone implant contact ratio (BIC). However, the most clinical studies on humans were reported the clinical survival rate. The results of the literature review are presented in Tables IV.

## IV. Discussion

Bone resorption and regeneration are continuously ongoing in the skeletal system due to the interaction of osteoblasts and osteoclasts. When a bone defect develops following trauma, surgery, or bone grafting, bone regeneration and resorption occur via this interaction of osteoblasts and osteoclasts.

The remodeling of bone involves the activation (A) of osseous precursor cells, leading to increased active resorption (R), quiescence or reversal of the activation (Q), and bone formation (F). These series of processes are referred to as the bone remodeling cycle. Each species, including humans, has a different cycle period. The cycle period is approximately 6 weeks in rabbits, 12 weeks in dogs, and 17 weeks in humans. The various stages are summarized in Table IV for rabbits, dogs, and humans.

The activation period lasts from a few hours to several days. After the resorption period, a quiescence period of variable duration occurs: a few days in rabbits, 1 week in dogs, and 12 weeks in humans. In the bone remodeling process, the bone formation period varies the most across species. In rabbits, dogs, and humans, it takes approximately 4.5, 10, and 13 weeks, respectively, and the time required for bone remodeling cycle is proportional to the size of animal. Assigning rabbits a relative size of 1, dogs require approximately twice the relative corresponding period, and humans require three times the corresponding period.<sup>40</sup>

In rabbits, woven bone appears on the implant surface, which becomes sufficiently dense within approximately 6 weeks; bone remodeling occurs, and it can sustain normal loading. Little quantitative data are available on the early healing process in humans, although based on the bone remodeling cycle period, it is estimated that the formation of the primary callus is similar to that in rabbits. Nevertheless, the maturation process in humans bone modeling takes approximately three times longer (approximately 18 weeks) compared to rabbits (Table V).

In animal experiments, it is difficult to evaluate the implant success rate, and the BIC rate is primarily measured, although radiological, histological, and histomorphometric analyses are also performed. Many reports have evaluated the bone formation rate with bone grafts using xenogenic or synthetic bone, and numerous recent reports have evaluated the use of platelet concentrated plasma. Regarding the time of animal death, minipigs are killed after 3, 6, 12, and 26 weeks,<sup>8,11</sup> rabbits after 2, 3, and 8 weeks,<sup>14</sup> and sheep after 12, 16, and 26 weeks.<sup>6,9,10,12,13</sup>

The initial studies of implants involved animal experiments. Linder and Lundskog<sup>41</sup> implanted a titanium cylinder in rabbit tibia under moderate loading, and noted that connective tissue intercalation was absent. Johansson and Albrektsson<sup>42</sup> placed screw-type implants in rabbits and reported that the adhesion of the bone and implant after 3, 6, and 12 months was 50, 65, and approximately 85%, respectively.

Most clinical studies of humans report primarily on the clinical success rate of implants, usually based on long-term follow-up. Boyne and James<sup>4</sup> performed the maxillary sinus floor lift procedure using autogenous bone; the implants were placed 6 months later, and they reported the first clinical results after a follow-up of 4 years.<sup>4</sup> In 1987, Misch<sup>43</sup> grafted a mixture of decalcified bone, blood, and tricalcium phosphate in the maxillary sinus and obtained a 98% success rate in 179 cases. In 1996, Blomqvist *et al.*<sup>15</sup> studied the success rate of immediate implant placement in 49 patients with 2 to 4 mm of residual bone and reported an 82% success rate with 314 implants after the 32 months follow-up. Unlike animal studies, many clinical studies have investigated the use of autogenous bones in maxillary sinus floor elevation. Autogenous bone is the best graft material for bone defects, and results in rapid bone formation and remodeling. The donor sites include the iliac crest, mandibular ramus, maxillary tuberosity, and mandibular symphysis, and bone powder, fragments, and sections can also be used. For cases with less than 2 mm of residual bone, autogenous bone grafts are recommended.<sup>44</sup> In 133 patients, Hrzeler *et al.*<sup>45</sup> placed the implants immediately after maxillary sinus floor

elevation in cases with more than 4 mm of alveolar crest, while they delayed placement for cases with less than 4 mm. At the 5-year follow-up, 98.9% of the implants were retained for a 90.3% success rate.

Animal studies of maxillary sinus floor elevation appear to be standardized in terms of the time of implant placement, time of animal death, and criteria used for the histological evaluation. Experimental studies of maxillary sinus floor elevation in sheep, pigs, and dogs are important precursors of clinical experiments.

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Table I . List of recent animal studies on maxillary sinus augmentation

References	Animal	No.	Materials	Results
Kirker-Head <i>et al.</i> (1997) <sup>5</sup>	goat	6	rhBMP-2.ACS	no complications
Hass <i>et al.</i> (1998) <sup>6</sup>	sheep	27	Bio-Oss, autologous bone	Autologous bone had significantly more BIC than the non-graft group.
Margolin <i>et al.</i> (1998) <sup>7</sup>	chimpanzee		collagen matrix OP-1	Bone formation was superior to that in the collagen matrix-alone group.
Terheyden <i>et al.</i> (1999) <sup>8</sup>	minipig	5	Bio-Oss, OP-1	The combination group (BIC 80%) was better than the Bio-Oss group (36%).
Haas <i>et al.</i> (2002) <sup>9</sup>	sheep	36	DFDB	The DFDB group required a slightly higher force than the non-augmented group in the pullout test.
Haas <i>et al.</i> (2002) <sup>10</sup>	sheep	27	HA autogenous bone	HA & autogenous bone group had more BIC than the non-grafted group.
Fürst <i>et al.</i> (2003) <sup>11</sup>	minipig	12	HA, PRP	PRP combined with HA was not superior to HA alone in terms of BIC.
Haas <i>et al.</i> (2003) <sup>12</sup>	sheep	27	HA, autogenous bone	The HA group had significantly more BIC than the non-grafted group.
Jakse <i>et al.</i> (2003) <sup>13</sup>	sheep	12	autogenous bone	The PRP group did not differ significantly in terms of BIC.
Butterfield <i>et al.</i> (2005) <sup>14</sup>	rabbit	12	autogenous bone	pQ-CT, fail

\*BIC: bone-implant contact; HA: hydroxyapatite; PRP: platelet-rich plasma; DFDB: demineralized freeze-dried bone pQ-CT: peripheral quantitative computed tomography; OP-1: osteogenic protein-1.

Table II. List of recent clinical studies on maxillary sinus augmentation (one stage)

References	Pt. no.	Imp no.	Graft material	Implant	D(mm)	L(mm)	Survival rate (%)
Blomqvist <i>et al.</i> (1996) <sup>15</sup>	49	171	iliac crest	Nobel Biocare AB			82.5
Khoury (1999) <sup>16</sup>	216	467	autograft	IMZ, Nobel Biocare, Branemark II Frialit-2		10-15	94
Johansson <i>et al.</i> (1999) <sup>17</sup>	39	131	iliac graft	Nobel Biocare AB	4	10, 13, 15, 18	95
Chanavaz (2000) <sup>18</sup>	982			Autograft, demineralized			99.34, 95.78
Artzi <i>et al.</i> (2002) <sup>19</sup>	10	36	Bio-Oss	Steri-Oss, Spline	3.7, 4.5	10-15	Success
Sartori <i>et al.</i> (2003) <sup>20</sup>	1		Bio-Oss	IMZ			86.7
Andreana <i>et al.</i> (2004) <sup>21</sup>	6	14	Capset	Paragon	3.75-4.7	10	No failure
Hatano <i>et al.</i> (2004) <sup>22</sup>	191	361	Bio-Oss, autogenous bone	Nobel Biocare	3.75-6	8.5-15	94
Engelke & Capobianco (2005) <sup>23</sup>	6	21	Cerasorb	Friadent, Xive	3.4-4.5	13-15	95.2
Simunek <i>et al.</i> (2005) <sup>24</sup>	24	45	algipore	Frialit-2	3.8	13	97.8

\*A: animal study; Imp: Implant; D: diameter; L: Length.

Table III. Human studies of maxillary sinus augmentation (two stage)

References	Pt. no.	Implant no.	2nd surgery (m)	Graft material	Implant	D (mm)	L (mm)	Survival rate (%)
Lozada <i>et al.</i> (1993) <sup>25</sup>	120	298	6	autogenous bone				85
Jensen <i>et al.</i> (1994) <sup>26</sup>	98	291	6	autogenous bone				93.5
Lundgren <i>et al.</i> (1996) <sup>27</sup>	10	30	6	autogenous bone	Nobel Biocare AB		10-18	100
Stephen <i>et al.</i> (1996) <sup>28</sup>	24	66	4-6	Bio-Oss,	IMZ, Branemark, 3i,			87
				autogenous bone	integral			Mix: 97
Yildirim <i>et al.</i> (2000) <sup>29</sup>	11	15	6.8	Bio-Oss	Nobel Biocare AB			89.5
van den Bergh <i>et al.</i> (2000) <sup>30</sup>	24	69	6	DFDBA	ITI	4.1		No failure
Wiltfang <i>et al.</i> (2000) <sup>31</sup>	53	132	6-8	Cerasorb			10-14	95
Hallman <i>et al.</i> (2002) <sup>32</sup>	21	111	6.5	Bio-Oss, autogenous bone	MarkII	3.75	10-15	Autogenous bone: 82 Mix: 94.3 Bio-Oss: 95.4
Scarano <i>et al.</i> (2004) <sup>33</sup>	1	3	10	Bio-Oss	Bicon			Bone contact 72
Hatano <i>et al.</i> (2004) <sup>34</sup>	191	361	6-9	autogenous bone, Bio-Oss (2:1)				94.2
Barone <i>et al.</i> (2005) <sup>35</sup>	18	36	5	Osteobiol, Autograft				No difference
Butz & Huys (2005) <sup>36</sup>	20	56	5-6	Autograft, Bioplant	Southern Implant			No failure
Gelbart <i>et al.</i> (2005) <sup>37</sup>	12	59	4	DFDBA				No failure
Deporter <i>et al.</i> (2005) <sup>38</sup>	70	104	4-6	bovine HA	endpore			98
Serra E Silva <i>et al.</i> (2006) <sup>39</sup>	10	33	6-11	autogenous bone Gen-Pro				Autogenous bone is better than Gen-Pro.

\*A: animal study; DFDBA: demineralized freeze-dried bone allograft; m: month; D: diameter; L: length

Table IV. Parameters of the bone remodeling cycle in rabbits, dogs, and humans

	Rabbits	Dogs	Humans
Activation (A)	<0.5	0.5	<1.0
Active resorption (R)	1.0	1.5	2.0
Quiescence of activation (Q)	0.5	1.0	1.5
Bone formation (F)	4.5	10.	13.0
A→R (Q) →F	6.0	12.0	17.0
Factor	1×	2×	3×

Table V. Differences in the bone remodeling process in rabbits and humans

Change in the bone	Rabbits	Humans (3×)
First step: Callus formation (weeks)	2	6
Second step: The deposition of lamellar bone (weeks)	6	18
Third step: Interface remodeling (weeks)	6	18
Fourth step: Bone maturation (weeks)	18	54

## 저작물 이용 허락서

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논문제목	한글 : 임프란트 식립을 위한 상악동 점막 거상술의 문헌고찰: 사람과 동물 연구				
	영어 : Review of human and animal studies on maxillary sinus grafting for implant placement				

본인이 저작한 위의 저작물에 대하여 다음과 같은 조건아래 조선대학교가  
저작물을 이용할 수 있도록 허락하고 동의합니다.

- 다 음 -

1. 저작물의 DB구축 및 인터넷을 포함한 정보통신망에의 공개를 위한 저작물의 복제, 기억장치에의 저장, 전송 등을 허락함
2. 위의 목적을 위하여 필요한 범위 내에서의 편집·형식상의 변경을 허락함. 다만, 저작물의 내용변경은 금지함.
3. 배포·전송된 저작물의 영리적 목적을 위한 복제, 저장, 전송 등은 금지함.
4. 저작물에 대한 이용기간은 5년으로 하고, 기간종료 3개월 이내에 별도의 의사 표시가 없을 경우에는 저작물의 이용기간을 계속 연장함.
5. 해당 저작물의 저작권을 타인에게 양도하거나 또는 출판을 허락하였을 경우에는 1개월 이내에 대학에 이를 통보함.
6. 조선대학교는 저작물의 이용허락 이후 해당 저작물로 인하여 발생하는 타인에 의한 권리 침해에 대하여 일체의 법적 책임을 지지 않음
7. 소속대학의 협정기관에 저작물의 제공 및 인터넷 등 정보통신망을 이용한 저작물의 전송·출력을 허락함.

동의여부 : 동의( ○ )    반대(    )

2009 년 2 월    일

저작자: 박 열 수 (서명 또는 인)

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