ISSN : 1001-1781
Journal of Clinical Otorhinolaryngology, Head, and Neck Surgery

THE COMPARISON OF THE EFFECTIVENESS OF DENSITY IN BONE HEALING PROCESS USING THE GRANULES TYPE OF SYNTHETIC BONE GRAFT SUBSTITUTE VERSUS WITHOUT USING THE GRANULES TYPE OF SYNTHETIC BONE GRAFT SUBSTITUTE IN MAXILLARY FRACTURE AT Dr. MOEWARDI GENERAL HOSPITAL : AN EXPERIMENTAL STUDY

Dewi Haryanti Kurniasih [1] , Rachmi Fauziah Rahayu Sp. Rad (K) N-KL[2] , Meily Anggreini [3]

[1] Cranio-Facial Consultant, Department of Plastic Surgery, Moewardi General Hospital, Surakarta, Central Java, Indonesia, [2] Head and Neck Neuroradiology Consultant, Department of Radiology, Moewardi General Hospital, Surakarta, Central Java, Indonesia
[3] Resident of General Surgery Specialist Program, Medical Faculty of Sebelas Maret University, Surakarta, Central Java, Indonesia

Background : The bone substitutes are being spreadly used in long bone but not in maxillofacial fracture, the reconstruction of maxilla itself was the 4th grade of the 10 most common treatment in the departement of plastic surgery in dr. Moewardi hospital (Aug-Oct 2022).[2,4] The benefits of synthetic bone graft is to reduce complications of infectious that can be transmitted by allografts, and the availability of materials in the market.[10] We attracted to research the difference in the effectiveness of density in bone healing between the use of synthetic bone substitute granule (SBSG) and without synthetic bone substitute granule (Non SBSG) in reconstruction of maxilla fractures at Dr. Moewardi Hospital.
Methods: This study is an experimental study, using *independent T Test* statistical study, and *consecutive sampling.* We compared 16 patient between the group reconstruction of *maxilla* using a granule type of synthetic bone *graft* substitute, and 16 patient in the group control. We evaluated the bone density in *hounsfield units* (HU) once in the period of 4 to 6 months after the reconstruction, using a Head CT scan.[8]
Result : The density of *maxillary* group reconstructed with the Synthetic Bone Substitute Granule (SBSG) is 618.06 HU, and 401.63 HU in the Group control. With p value < 0.001 (signifikan p < 0.05), its mean the hypothesis has been proved. We also found that there is no significantly differences between the each group based on age and gender.

Finding : The defects with minimum sized 0.5 cm was filled with bone graft substitute, as a bridging, the materials have properties of *osteoconduction* to conjunct the osteoblasts on the edges of defects to spread and form a new bone and *osteoinduction* to stimulate the *osteopregenitor.*[1,3] Those two roles combine with *osteogenesis* in the remodeling phase, at 4-6 months after surgery, which form high bone density.[11]

INTRODUCTION

Maxillary fractures are fractures of the facial bones which are more common than the other facial bone fractures. Based on a study conducted by Rowe and Killey in 1995, the ratio

between fractures of the maxilla and mandible exceeded 4:1, some recent studies conducted in trauma units of hospitals in several countries showed that the incidence of maxillary fractures was more than mandible fractures. Other data were also reported from level one trauma centers that among 663 patients with facial bone fractures, 25.5% were maxillary fractures. [25]

The incidence of maxillary fractures at Dr. Moewardi Hospital treached 131 cases in 1 year (January 2019 to December 2019), which most of cases were caused by motorized vehicle accidents.[11] With this high incident rate, the management of maxilla fracture continues to develop in an effort to provide the best goals for patients.

The rigid internal fixation on a functionally stable bone surface and the size of the gap in the fractured bone are known as a factors that affect the healing of craniomaxillofacial bones contained in the basic principles of AO/ASIF (Arbeitsgemeinschaft Osteosynthesefragen / Association for the Study of Internal Fixation) of craniomaxillofacial surgery, apart from the other factors which are surgical application and vascularization. [32]

Reconstruction of maxilla fractures with bone defect are start from the arranged of bone fragments, repositioned and reduced the fracture bone, and then maintaining immobilization with internal fixation. In the last 2 decades, the provision of bone grafts for reconstruction has also developed. After immobilization is achieved, the defect was filled with bone grafts as an effort to reduce the size of the gap, to accelerate and stimulate the growth of new bone.

However, there is a problem of supply availability for both autografts and allografts that makes researchers interested in finding substitute materials. A study conducted by Andries Pascawinata et al., it was explained that the synthetic bone graft material is as good as natural material in a function of bone graft.[34] In a study by William R. Moore et al said, in the last 30 years it is known that synthetic bone grafts have other benefits, namely in terms of reducing infectious complications that can be transmitted by allografts or autografts apart from the availability of materials, reducing patient morbidity is particular value for the relevance of synthetic bone graft.[35]

Several studies have been carried out on the use of synthetic bone grafts for long bones, but only a few for the *maxillofacial* bones. While its use quite often in RSUD dr. Moewardi, both in long bone and *maxillofacial* surgery. This research was conducted to assess the maxillary bone reconstructed by administering synthetic bone graft in terms of bone density, so it is hoped that its use in *maxillofacial* fractures will be wider. [14]

RESEARCH METHODS

Synthetic Bone Substitute Granule (SBSG)

Synthetic bone substitute granule Is a non-structural bioactive bone graft that contains Hydroaxyapatite (HA), Calcium Phospate (CP), and Synthetic Calcium Sulphate (CS) with varying particle sizes in the form of granules. The graft was filled to the bone defect after the bone was fixed with a plate and screw.

Without Synthetic Bone Substitute Granule (Non SBSG)

Reconstruction using a plate and screw (Fig 1) in a fracture of maxilla without applied synthetic bone graft on bone defects.

The bone defect size in the both group is 0.5 - 1 cm.

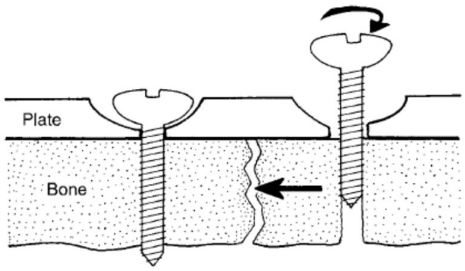


Figure 1. The screw hole mechanism fixation, independently compresses the plate.

Patients and Methods

This research is an experimental study in which the researcher treats the research subjects. The design is an experimental post test control design only, it compare the group with experiment, and the group that wasn't given the experiment.

After the ethical clearance (EC) arrangements (EC No. 825/VI/HREC/ 2020), researchers start to collect patient medical record, with a history of reconstruction maxilla fracture using SBSG or without SBSG, operation report, and preoperative head ct scan.

The samples was carried out at The Medical Record Departement in RSUD Dr. Moewadi Surakarta, for two years (January 2020 – January 2022). With the Inclusion and exclusion criteria :

1. Inclusion criteria
a. Patient pasca reconstruction maxilla with SBSG.
b. Patient pasca reconstruction maxilla without SBSG.
c. Maxillary complex fracture patients (multiple, communited, complete, complicated, depressed).
d. Maxilla fracture patients were aged 10 to 60 years.
e. Maxilla fracture patients without history of systemic and chronic disease.
f. Maxillary fracture patients without infection of internal fixation.
g. Maxillary fracture patients with related injury of trauma
2. Exclusion criteria
a. Simple fractures maxillary (incomplete).
b. Patients who refuse CT Scan Evaluation.
c. Maxillary fracture without bone defects.
d. Maxillary fracture caused by non trauma case.

The inclusion criteria group will be measured for bone density examination with Ct Scan Radiology, the study was examined on the 4 months after surgery. The density in normal bone is 500 - 2000 Hounsfield Unit (HU), and for bone grafts is 100 – 400 HU.[31]

The data were tested using independent T Test to assess differences in the outcome of operations. Shapiro Wilks Normality Test for sample < 50 and Levene Test for homogeneity of variance. The data were processed using SPSS for windows 22.0. A p value > 0.05 is no significants, $p \leq 0.05$ is significants, $p < 0.01$ is highly significants.

RESULTS

The Characteristics of Research Subjects

This research was conducted at Doctor Moewardi General Hospital from January 2020 to January 2022. This is an experimental study with posttest-only control group design, it was comparing between the two groups where the reconstruction of maxillary fracture group with SBSG, and the group without SBSG, to determine the effectiveness in density of reconstruction maxillary fractures with bone defects using SBSG.

The secondary data taken from medical records patients at dr. Moewardi Hospital Surakarta, on January 2020 to January 2022, the data contained patient identity, history of bone fractures, history of surgery, CT scan photos before surgery and after surgery. We used the consecutive sampling technique, obtained a sample of 32 subjects, and devided in 2 group, each group has 16 patients in a group of reconstruction maxillary fracture with SBSG and 16 patients in a group of reconstruction maxillary fracture without SBSG .

An overview of the basic characteristics research subjects can be seen in table 1 as follows.

Tabel 1 Characteristics of Subjects Research

Characteristics	Group		p-value
	SBSG (n=16)	Non SBSG (n=16)	
Gender [a]			0.264
Men	9 (56.3%)	12 (75.0%)	
Women	7 (43.8%)	4 (25.0%)	
Age[b]			0.595
Mean ±SD	27.19 ±9.99	26.81 ±8.27	

Noted: [a] unpaired different group test nominal categorical data with chi sqaure test, [b] unpaired different group test numerical data were not normally distributed with the Mann Whitney test. *)significant if p<0.05

Based on table 1, it is known that the gender patients in the SBSG group has the proportion mostly male, namely there are 9 patients (56.3%), in the SBSG group, the proportion of patients in Non-SBSG group is also mostly male, namely there are 12 patients (75.0%). The statistical test results obtained a p value = 0.264 (p> 0.05) which means that there was no significant difference in the characteristics of the study subjects based on gender between the SBSG group and the Non-SBSG group.

The average age of patients in the SBSG group was 27.19 years with a standard deviation of 9.99 years (27.19 ± 9.99 years), with a minimum age is 14 years and a maximum age is 56 years, and in the Non-SBSG group an average age is 26.81 years with standard deviation is

8.27 years (26.81 ± 8.27 years), with a minimum age is 14 years and a maximum age is 37 years. The statistical test results obtained a p value = 0.595 (p> 0.05) which means that there was no significant difference in the character of the research subjects based on age between the SBSG group and the Non-SBSG group.

Variance Normality and Homogeneity Test

Based on Shapiro Wilk Test, the distribution of data from measurements of maxilla fracture reconstruction with bone defects (Ct Scan) in both sample group met the assumption of normality with a p>0.05 value. The normality test results can be seen in table 2 as follows.

Table 2 *Shapiro Wilk* Normality Test

Group	Maxilla Fracture Reconstruction			Information
	Statistics	df	p-values	
SBSG	0.959	16	0.642	Normal
Non SBSG	0.954	16	0.564	Normal

Noted: *Shapiro Test* ; Normal if the value of p> 0.05

The results of the homogeneity test between 2 groups can be seen in table 3 as follows.

Table 3 Homogeneity Test

Levene Statistics	p-values
1,981	0.170

Noted: *Levene Test* ; homogeneous if the value of p> 0.05

The results of the homogeneity test based on the Levene Test, showed that the variance of measurement results for maxilla fracture reconstruction with bone defects between a group using SBSG and a group without using SBSG is reported as a value of p=0.170 (p>0.05), which means homogen.

The Effectiveness of Bone Healing Density

The effectiveness of bone healing density after reconstruction of maxilla using internal fixation accompanied by Synthetic Bone Substitute Granule (SBSG) or Without Synthetic Bone Substitute Granule (Non SBSG) was carried out using the independent t test because the data met the assumption of normality. The results can be seen in table 4 as follows.

Table 4 The Differences Results of Bone Density in Maxilla Fracture Reconstruction with Bone Defects Between SBSG and Without SBSG Groups

Variable	Group		p-values
	SBSG (n=16)	Non SBSG (n=16)	
Maxilla Fracture Reconstruction (Ct Scan - HU)			<0.001*
Mean ± SD	618.06 ± 82.72	401.63 ± 55.59	

Noted: Differences test in unpaired groups of numerical data passed the normality requirements (Independent t test) . * Significant if p<0.05.

Based on table 4, the average value in a group with SBSG was 618.06 HU with a standard deviation of 82.72 (618.06 ± 82.72). And in a Group without SBSG, the average value was 401.63 HU with a standard deviation of 55.59 (401.63 ± 55.59), which we can see in the diagram below.

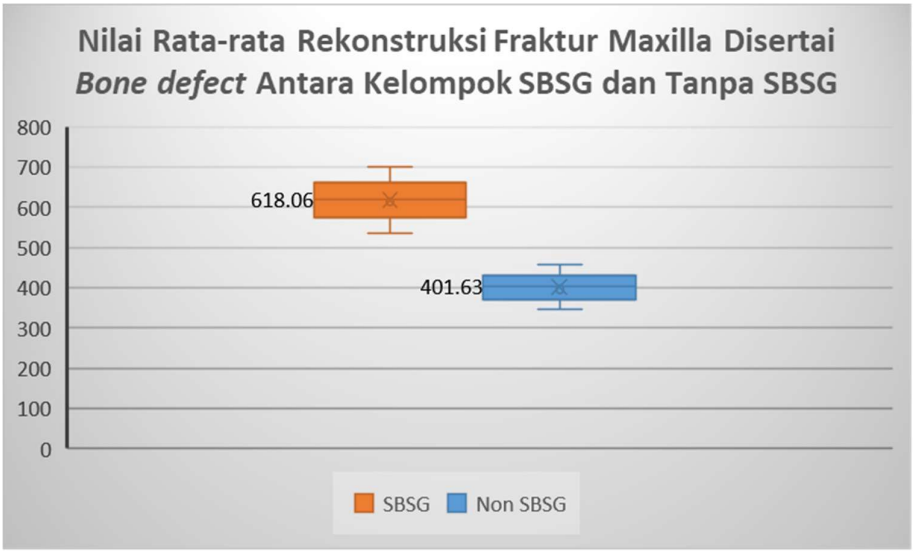


Figure 2. Box Plot Diagram for Reconstruction of Maxilla Fracture with Bone defects between the SBSG and Non SBSG groups

The statistical results for each group obtained p = <0.001 (p <0.05) which means that there was a significant difference of bone density (HU) between a SBSG Group and Non-SBSG Group. Patients who undergo the maxilla reconstruction with addition of SBSG on the bone deffect has higher bone density than without the addition of SBSG. The hypothesis can be proven which states "There is a difference in the effectiveness of bone healing density between the use of Synthetic Bone Substitute Granule (SBSG) and Without Synthetic Bone Substitute Granule (Non SBSG) in the reconstruction of maxilla fractures with bone defects at Dr. Moewardi General Hospital."

DISCUSSION

Bone grafting is a surgical procedure that uses transplanted bone to repair and rebuilt desease or damaged bones. The transplanted bone can be taken either from the patient it self (autograft), from donor bone (allograft), or from synthetic materials. [18]

A Synthetic Bone Graft Substitute is a non-structural bioactive bone graft that contains Hydroxyapatite (HA), Calcium Phosphate (CP), and Calcium Sulphate (CS), combined with mineral ingredients, ions, and growth factors such as bone marrow aspirate and strontium.[8,18]

A calcium phosphate has high biocompatibility, high porosity, fast absorption, and osteoconducting activity.

This study was used Hydrociapatite (A calcium phosphate), it has high biocompatibility, high porosity, similiar to inorganic phase of bone, and osteoconductive properties. A calcium phosphate is a bioresorbable material, it resorbs in aproximately 13-20 weeks after implantation and is then completely replaced by remodeled bone, so that we evaluate on 16 weeks after implantation. The new bone regeneration after HA bone substitute grafting was measured as the presence of newly formed bone (histomorphometric), bone density (radiographic), or bone defect fill (radiographic or bone sounding methods). in this study we measure the bone density, which was evaluated independently by one readers, a head and neck radiology consultant.[33,37]

In another study, Beta-tricalcium phosphate (b-TCP) and hydroxyapatite (HA) had high purity, and chemical compositions with predictable biological effects. TCP and HA ceramic granules have shown a correlation between bone replacement resorption and bone regeneration depending on the density and purity of the bone graft ceramic material, defect size, implant, and capability of osteogenetics in each patient. [33]

There are various forms of synthetic bone graft preparations, ranging from porous blocks, granules, and pastes cement, as we can see in Figure 3. In this study, a granules synthetic bone graf (Figure 4), were placed on the defect or filled in the bone gaps after being reduced and internal fixation.

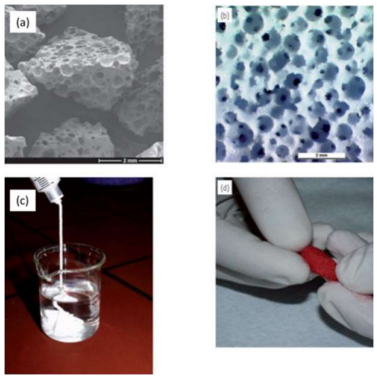


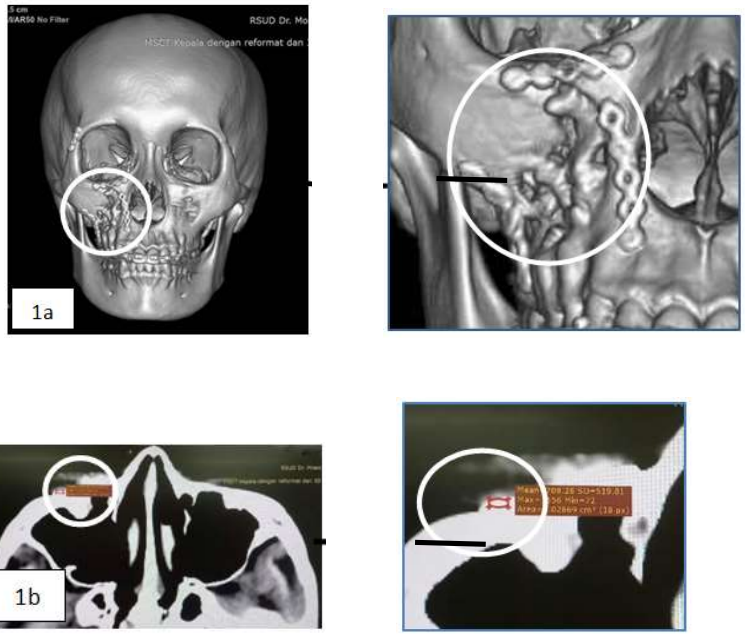
Figure 3. Four main forms of bone graft substitutes: (a) Granule ; (b) Block ; (c) hydraulic cement–injectable paste; (d) putties. With a pore size range of 0.1 – 1.0 mm. [6]

Figure 4 . Synthetic Bone Substitute Granule (SBSG)

In the bone healing, with the principle of minimal movement, through several stages of repair in the form of increasing mechanical strength as simultaneously, namely, hematoma and inflammation, callus formation, replacement by woven bone, and finally remodeling into flat or trabecular bones. When there is direct bone apposition and compression of small rigid spaces, healing occurs more rapidly because the initial repair stage is minimized or eliminated. The best achievement of bone healing in the remodeling phase is achieved in the 4th to 6th month after the procedure, so we conducted an assessment in that time frame. [33]

Synthetic bone graft substitute has osteoconductive and osteoinduction properties. Osteoconductive is the process of connecting the growth of natural bone, where osteoblasts from the edge of the defect will use the bone graft as a framework to spread and form new bone. Osteoinductive is the process of converting undifferentiated cells into active osteoblasts so that they will differentiate. This stimulates the osteoprogenitor to differentiate into osteoblasts in osteogenesis to initiate new bone formation.

In this study, the authors measured the density of maxillary bone using a ct scan device in the number of Honsfield units (HU). Then compare the bone density values of the two groups (Figure 5).



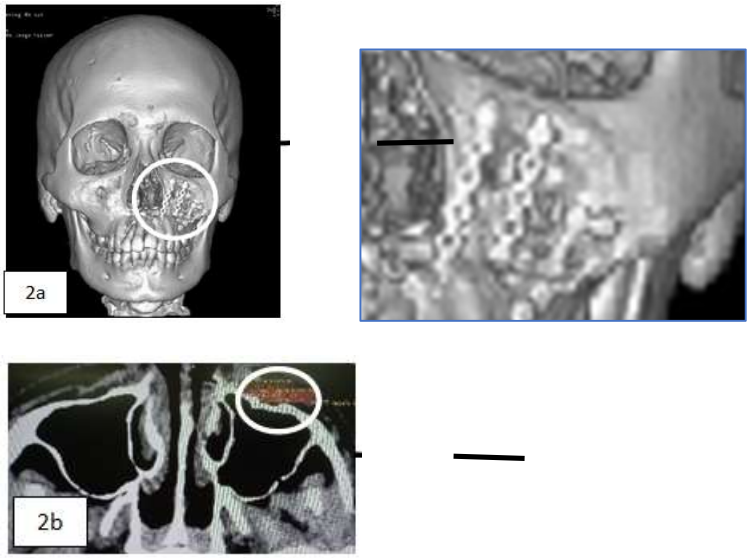


Figure 5. Head CT Scan Post Maxillary Reconstruction With SBSG and Without SBSG : (1 a) 3D CT Post reconstruction with SBSG ; (1b) Axial view for calculating hounsfield units ; (2a) 3D CT Post reconstruction Without SBSG ; (2b) Axial view for calculating hounsfield units.

The results of maxillary reconstruction in a SBSG group, the mean bone density was 618.06 HU. And the result of a maxilla reconstruction without SBSG group was 401.63H. The statistical value for the differences result of Ct Scan between a SBSG group and without SBSG group was obtained a p value =<0.001 ($p<0.05$), which means that there was a significant difference in the results.

CONCLUSION

The results of bone density in the healing process of post-reconstruction maxillary patient with SBSG were higher than patient of post-reconstruction maxillary without SBSG.

ACKNOWLEDGEMENTS

We would like to acknowledge our institution, Faculty of Medicine, Universitas Sebelas Maret Surakarta, for the support and funding. In addition, we express our gratitude to all the patients in this study.

AUTHOR CONTRIBUTION

Dewi Haryanti K: Writing the manuscript and the first author. Meily Anggreini: Designing and corresponding author.

REFERENCE

[1]Mohammed E. Elsalanty, and David G. Genecov, 2009. Craniomaxillofacial Trauma & Reconstruction/Volume 2, Number 3/4.

[2]Greenberg A. M., dan Prein J., 2002, Craniomaxillofacial Reconstructive and Corrective Bone Surgery, *Principles of Internal Fixation Using the AO/ASIF Technique*, Springer-Verlag New York, Inc.

[3]Zhao, J., Zhiyuan, Z., Shaoyi, W., Xiaojuan, S., Xiuli, Z., Chen, J., Kaplan, D., dan Jiang, X., 2009, Apatite-Coated Silk Fibroin Scaffolds To Healing Mandibular Border Defects In Canines, *Bone* 45, Elsevier, p : 517–527.

[4]Rimondini, L., Nicolò, N-A., Milena, F.,Gaetano G.,, Matilde, T., dan Giardino, R., 2004, In Vivo Experimental Study On Bone Regeneration In Critical *Bone defect*s Using An Injectable Biodegradable PLA/PGA Copolymer. *Oral Surgery, Oral Medicine, Oral Patholog,.* Bologna : Instituti Ortopedic Giardino.

[5]Van Gaalen S, Kruyt M, Meijer G, Mistry A,Van Den Brucken J, Jansen J., De Groot K., Cancedda R., Olivo C., Yaszemaski M., dan Dhert W., 2008, Tissue Engineering of The Bone, *Tissue Engineerring*, Blitterswijk, C (eds), Elsevier, San Diego, p : 560.

[6]Othsuki M., 2009, Bone-grafting Materials Their Uses Advantages and Disadvantages, *The Journal of the American Dental Association*, Vol. 133.

[7]Wataha, J.C., 2001, Principles of Biocompatibility for Dental Practitioners, *The Journal of Prosthetic Dentistry*, 86 (2), p : 203-209.

[8]Bronzino, J. D., 2006, Tissue Engineering and Artificial Organs, 3rd edition, CRC Press.

[9]Smeltzer, S.C & Bare, B.G, 2002. Buku Ajar Keperawatan Medikal Bedah (Ed.8) Jakarta:EGC.

[10]Meeker & Ronthrock, 1999. Care on the patient in surgery. Eleventh edition, Mosby, Inc St Louis, Baltinore.

[11]Arosarena Oneida A, MD, et al. 2009. Maxillofacial Injuries and Violence Against Women. Arch Facial Plast Surgery. 2009; 11(1):48-25.

[12]Werning John W, MD, et al. 2004.The Impact of Osteoporosis on Patients With Maxillofacial Trauma. Arch Otolaryngol Head Neck Surg. 2004; 130:353-356.

[13]Fraioli Rebecca E, MD,et al. Facial Fractures: Beyond Le Fort. Otolaryngol Clin N Am.2008; 41:51-76.

[14]Alcala-Galiano Andrea, MD, et al. Pediatric Facial Fractures: Children Are Not Just Small Adults. Radiographics. 2008; 28:441-461.

[15]Kemenkes RI 2013. Riset Kesehatan Dasar:RISKESDAS. Jakarta:Balitbang

Kemenkes RI.

[16]Smith, H.L. 2011. Epidemiology And Clinical Indicators Of Midface Fracture In Patients With Trauma. The University of Iowa.

[17]Cole A, et al. Principles of fractures. In: Apley's System of Orthopaedic and Fractures.9th ed. 2010. Hodder arnold UK company. P.687.

[18]Laurencin,C.T.2006. Bone Graft Subtitutes. Availableat: http://www. emedicine.com/orthoped/ topic611.htm.

[19]N Hossain, M Barry.Management of Traumatic Bone Loss.The journal of bone and joint surgery. 2011.

[20]Black Joice M& Jane Hokanse Hawks. 2014. Medical Surgical Nursing Vol/21/ Jakarta:Salemba Medika.

[21]Bare B.G., Smelzer S.C. 2013. Buku Ajar Keperawatan Medical Bedah. Jakarta:EGC.

[22]Kahle Leonhardt Platzer, alih bahasa Syamsir HM. 1997. Atlas Berwarna & Teks Anatomi Manusia Sistem Lokomotor Muskuloskeletal & Topografi, Jilid 1 Edisi 6 yang direvisi, Hipokrates, Jakarta.

[23]Moore, K.L., Dalley, A.F., Agur, A.M. 2014. Moore Clinically Oriented Anatomy Seventh Edition. p: 822-859

[24]Sjamsuhidajat and Wim de jong. 2011. Buku Ajar Ilmu Bedah. Edisi 3. Jakarta:EGC.

[25]Subhod S.Nathu, Harsha Pradhian.2014. An Epidemialogical Study on Patern and Incidence of Mandibular Fraktur in Plastic Sugerry International. Accsed 6 Agustus 20014. Available at http://wwwdx.doi.org/101155/2012/ 834364.

[26]Dahlan, M.S. 2016. Besar Sampel Dalam Penelitian Kedokteran Dan Kesehatan. Jakarta:Epidemiologi Indonesia.

[27]Notoatmodjo, Soekidjo. 2010.Metodologi Penelitian Kesehatan.Jakarta:Rineka.

[28]W. Zhu, Q. Ma, S. Borg, C. Öhman Mägi, X. Weng, H. Engqvist and W. Xia, J. An. . 2019. Article : Journal of Material Chemistry. DOI: 10.1039/C9TB00238C.

[29]Kumar, Prasanna, Vinitha, Belliappa, Fathima Ghousia.2013. Journal of Pharmacy & Biollied Sciences: Bone Graft in Dentistry. Departement of Oral and Maxillofacial Surgery, Bhabha College of Dental Sciences, Bhopal, Madhya Pradesh, India.

[30]W. Zhu, Q. Ma, S. Borg, C. Öhman Mägi, X. Weng, H. Engqvist and W. Xia, J. Mater. Chem. B, 2019.Journal of M aterials Chemistry B. DOI: 10.1039/C9TB00238C.

[31]Grottoli, Carlo F. et all. 2019. An Article: A Radiological Approach to Evaluate Bone Graft Integration in Reconstructive Surgeries. Radiologia Diagnostica Presidio CTO, Azienda Ospedaliero-Universitaria Città della Salute e della Scienza di Torino, 10129 Torino, Italy.

[32]Greenberg, Alex M. Et all. 2002. Craniomaxillofacial Reconstructive and Corrective Bone Surgery: Principles of Internal Fixation Using the AO/ASIF Technique. Craniomaxillofacial Bone Healing, Biomechanics, and Rigid Internal Fixation. Kummer, Frederick J.

[33]Raphael Bettach, DDS. Et all.2014. Clinical Performance of a Highly Porous Beta – TCP as the Grafting Material for Maxillary Sinus Augmentation. DOI: 10.1097/ID.0000000000000102.

[34]Pascawinata, Prihartiningsih, Dwirahardjo.Perbandingan Proses Penyembuhan Tulang antara Hidroksiapatit nanokristalin dan Hidroksiapatit Mikrokristalin. Bagian Bedah Mulut & Maksilofasial, FKG, Universitas Gadjah Mada, Yogyakarta.

[35]Moore, et all. Synthetic Bone Graft Substitutes. Department of Orthopaedic Surgery, Modbury Public Hospital, Modbury, Department of Orthopaedics and Trauma, Royal Adelaide Hospital, Adelaide, South Australia, Australia.

[36]Canale S. Terry, Beaty JH. 2013. Campbell's Operative Orthopedics. 12th Edition. Elsevier.

[37]Grado Gabriel F, Et all. 2018. Journal of Tissue Engineering. Bone Substitute : a review of their characteristics, clinical use, and perspective for large bone defect management. DOI :10.1177/2041731418776819.