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RESEARCH CENTER FOR BIOMEDICAL DEVICES

AND PROTOTYPING PRODUCTION

Integration of development on

Biomate Dental Implant System

Applicant : Biomate Medical Devices Technology Co., Ltd.

Test Article : Biomate Dental Implant System

Test Period : 2013/12/01～2015/05/06

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Test Article: Biomate Dental Implant System

Applicant : Biomate Medical Devices Technology Co., Ltd.

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Report Title

Integration of development on Biomate Dental Implant System

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Approval

Taipei Medical University
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1. Purpose

The Dental Department at Taipei Medical University Hospital is conducting a human trial by inserting Biomate dental implant system in edentulous patients (TMU-JIRB No. 201301009), having the physicians observe for any signs of immune rejection afterwards, and questioning the patients in regards to the adaptation and the recovery state from the implants. The patients are asked to return to the clinic each month after the implant is placed. The successfulness of the implant insertion is assessed by intraoral palpation, x-ray imaging, computed tomography (CT), and the dental implant stability quotient (ISQ) is measured by an implant stability meter. The success rate of the implantation is statistically analyzed 6 months post-surgery. The present trial is a pilot study to assess the efficacy and safety 6-month post implantation.

2. The Investigators and the Study Site

Investigators: Chiung-Fang Huang, Chia-Yu Wu.

Study Site: Dental Department, Taipei Medical University Hospital.

3. Trial Period and Guideline

3.1 Trial Period

Trial Start Date	12/20/2013
Trial End Date	05/06/2015
Report Issue Date	09/15/2015

3.2 Trial Guideline

Subject demographic and the data from the artificial dental implant trial are analyzed.

4. Methods and Materials

4.1 Test Object

Biomate Dental Implant System, Ministry of Health and Welfare approval number: DOH-Med-Device-MFG No. 003493.

Coloring management system is implemented on the exterior packaging. Blue, green, purple, and orange-colored labels are attached to the exterior packaging to indicate the diameter as ϕ3.3, ϕ4.1, ϕ4.8, and ϕ5.5, respectively. In addition, the length of the implant body is also specified on the labels (8, 10, 12, and 14 mm).

4.2 Equipment

❶Surgical instruments for dentistry

❷X-ray machine

❸CT scanner

❹ISQ meter

4.3 Trial Design

This is an open, parallel-designed trial. Subjects to be enrolled are edentulous patients with missing 4th (first premolar), 5th (second premolar), 6th (first molar), or 7th (second molar) tooth in the posterior zone of the upper or lower jaws to receive artificial dental implant in the trial. Each subject is to receive the maximum of three implants in order to learn the success rate of the product. A total of 40 subjects are to be enrolled. The subjects are allocated as follows:

❶10 younger male patients aged 20~45 years old.

❷10 younger female patients aged 20~45 years old.

❸10 middle aged and elderly male patients above 46 years old.

❹10 middle aged and elderly female patients above 46 years old.

Figure 1. Study Design

4.4 Study Procedures

General dental surgery for dental implantation is used in the present trial. X-ray imaging and CT scans are conducted prior to the dental implantation (Week 1) to confirm the implant location during the treatment period; prior to the insertion of the implant and the suturing of the wounds, the patients are anesthetized, flap incised, and implant hole pre-drilled. Observation, suture removal, and the fabrication of the crown are conducted during the observation period (please refer to Table 1, and Figure 2 of the surgical flowchart). The implants used in the present trial are permanent implants. Removal is not needed if the subjects do not experience any adverse effects. The course of treatment for one subject is 6 months. 4 Subjects are scheduled each week, for a total of 40 subjects. As 12 weeks of time is needed to complete the Week 1 study, the duration of the trial is 12 months.

The success and failure criteria of the implants are determined by the actual trial status; the criteria are further described below:

(1) Implant success criteria

The definition proposed by Alrektson and Smith, and Zarb and the actual condition as determined by the present study are as follows:

1. Each patient should have detailed medical records from the scheduled follow-up visits, complete pre-surgery, post-surgery, and follow-up x-ray records (periapical films and panoramic x-ray).
2. All dental implants are Biomate Dental Implant System manufactured by Biomate Medical Devices Technologies Co., Ltd, Taiwan, between 2013 and 2014. The device is approved by the Ministry of Health and Welfare, approval number: DOH-Med-Device-MFG No. 003493. The trial is conducted at the Dental Department of Taipei Medical University Hospital.
3. Well-trained implant dentists and nurses conduct the surgery. Experienced prosthetic specialists and technicians fabricate the implant prostheses.
4. The implantation is determined successful when the implant is stable in the alveolar bone, fixed, without causing pain starting from the insertion of the implants into the alveolar bone, to the attachment of the prosthetics, to the initiation of chewing, and finally to the completion of the trial.

(2) Implant failure criteria

1. The implantation is determined as failed when the implant is moving and causing pain to the patients when the implant or the prosthesis is palpitated or percussed, or during chewing in clinical examination.
2. Implantation is determined as failed in the presence of extensive radiation transmission lesions in x-ray imaging, and the alveolar bone resorption surrounding the implant is more than half of the implant depth.

(3) Records of implant complications and symptom criteria

1. Soft tissue pain

Plaque build-up round the implants causing the inflammation of the soft tissues surrounding the implants. The implant is determined as fail if the implant or the prosthetic is fixed or does not cause pain upon palpitation or percussion.

2. Pain from the dental implant

The implant is considered failed if pain from the dental implant is found.

(4) Amplitude of implant mobility

The mobility is categorized into using a 4-score scale ranging from 0-4:

Scale 0：Absence of clinical mobility from any direction

Scale 1：Slight detectable horizontal movement

Scale 2：Moderate visible horizontal mobility < 0.5mm

Scale 3：Severe horizontal mobility > 0.5mm

Scale 4：Vertical movement

Implant is determined as failure in the presence of implant movement, i.e. Scale 1 and above.

Table 1. Treatment Process

Treatment Procedure	Treatment	Detail
Screening	X-ray imaging Establishment of demographic information Explanation of the treatment procedures	Oral assessment and treatment procedure explanation, establishment of subject demographic database.
Treatment Period	Pre-surgical x-ray imaging Pre-surgical CT scan Implantation Post-surgical x-ray imaging ISQ meter Receive analgesics	Confirmation of the location. Administration of anesthesia, incision of the flap, and the placement of the implant according to the treatment procedures of Biomate Dental Implant System. X-ray imaging and CT scanners are used to assist the treatment.
Suture Removal	Suture removal ISQ meter X-ray imaging	Suture removal. X-ray imaging and ISQ meter are used to observe and record post-implantation recovery.
Observation Period	X-ray imaging CT scan ISQ meter Crown installation	Observation and recording of patient recover from the implantation using x-rays, CT scans, and ISQ meter. The crown is installed based on the state of recovery.

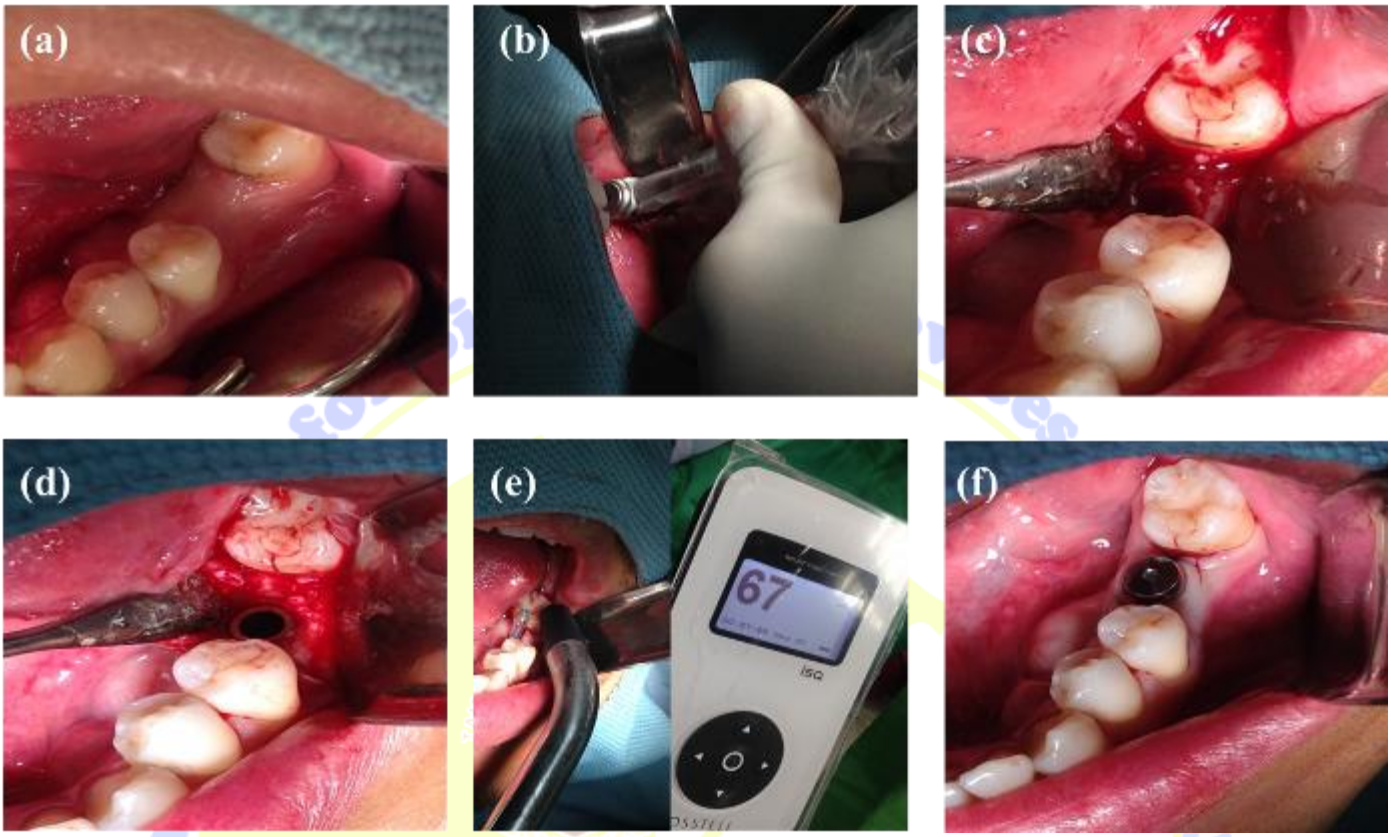

Figure 2. Implantation Procedures

5. Results

5.1 Demographic Analysis

40 Volunteers were recruited during the study period in accordance to the protocol for the placement of Biomate Dental Implant System. From the demographic data, there were 10 male and 10 female subjects in the 20 to 45 years old group; there were also 10 male and 10 female subjects in the 46+ years old group. The age distribution for the male subjects is 24 to 64 years old, mean age is 43 years old (±13.7); the age distribution for the female subjects is 23 to 63 years old, mean age is 44 years old (±12.6). A total of 60 Biomate Dental Implant is placed in the present trial with 15 implants in the upper jaw, occupying 25% of all the implants, and 45 implants in the lower jaw, occupying 75% of all implants.

The initial ISQ observed ranged from 48 to 85, with the mean of 67.9(±8.4). Week 8 ISQ ranged from 53 to 80, with the mean of 71.4(±6.3). Week 12 ISQ ranged from 57 to 83, with the mean of 71.1(±6.6). Week 16 ISQ ranged from 60 to 91, with the mean of 74.4(±8.1).

The pre-surgery bone mineral density (BMD) of the edentulous zone ranged from 200 to 1019, with the mean of 565.7(±207.8). Week 4 BMD ranged from 352 to 1205, with the mean of 851.8(±206.3). Week 16 BMD ranged from 402 to 1150, with the mean of 867.1(±193.6).

5.2 Statistical Analysis of the Artificial Dental Root Trial

The implanted jaw or the dental zone was cross analyzed with the gender and the age group of the subjects (Tables 2 and 3). No statistical difference ($P > 0.05$) was found in terms of gender. The ratio of placing implants in the mandible in male subjects was 81.3%, which is higher than that of the female subjects at 67.9%. The ratio of placing implants in the molars in male subjects is 93.8%, which is higher than that of the female subjects at 67.9%.

Statistical significant difference ($P < 0.05$) was found in the placement of jaws in terms of age group. The ratio of placement of the implants in the mandible in patients above the age of 46 is 78.8%, which is higher than patients between 20 to 45 years old, at 70.4%. In terms of dental zone in different age groups, the ratio of placement of the implant in the molars for subjects above 46 years old is 75.8%, which is lower than the 88.9% in the 20 to 45 years old group.

Table 2. Gender and Subject Oral Demographics Cross Analysis

	SEX					
	Female		Male		Total	
Jaw						
Palate	9	60.00%	6	40.00%	15	100.00%
Mandible	19	42.00%	26	58.00%	45	100.00%
Total	28		32		60	100.00%
Tooth area						
Premolar	9	82.00%	2	18.00%	11	100.00%
Molars	19	39.00%	30	61.00%	49	100.00%
Total	28		32		60	100.00%

Table 3. Age Group and Subject Oral Demographics Cross Analysis

	Age					
	20~45years		Over 46 years		Total	
Jaw						
Palate	8	53.30%	7	47.00%	15	100.00%
Mandible	19	42.00%	26	58.00%	45	100.00%
Total	27		33		60	100.00%
Tooth area						
Premolar	3	27.30%	8	72.70%	11	100.00%
Molars	24	49.00%	25	51.00%	49	100.00%
Total	27		33		60	100.00%

Week 1 ISQ after the implantation was explored (Table 4). The result showed no statistical difference ($P > 0.05$) in terms of gender and age group. The mean ISQ value for female subjects in Week 1 is 66.36 （±5.71）, while that of the male subjects is 68.90（±9.57）. The mean value for subjects between 20 to 45 years old is 65.15（±12.86）, while that of the subjects above 46 years old is 68.56（±8.52）.

The results of Week 8 ISQ (Table 5) showed no statistical difference ($P > 0.05$) in terms of gender

and age group. The mean ISQ value for female subjects is 70.77(±6.25), while that of the male subjects is 71.87 (±6.53). The mean value for subjects between 20 to 45 years old is 74.00 (±4.31), while that of the subjects above 46 years old is 69.91 (±6.94).

The results of Week 12 ISQ (Table 6) showed no statistical difference (P > 0.05) in terms of gender and age group. The mean ISQ value for female subjects is 65.85 (±10.04), while that of the male subjects is 70.83 (±7.09). The mean value for subjects between 20 to 45 years old is 70.37 (±6.97), while that of the subjects above 46 years old is 67.04 (±9.71).

The results of Week 16 ISQ (Table 7) showed no statistical difference (P > 0.05) in terms of gender and age group. The mean ISQ value for female subjects is 76.59(±8.73), while that of the male subjects is 72.68 (±7.29). The mean value for subjects between 20 to 45 years old is 71.31 (±7.17), while that of the subjects above 46 years old is 76.98 (±5.54).

Table 4. Week 1 ISQ and Subject Demographics Analysis

	Number	Average	Standard deviation	Median	(Q1,Q3)	T-Value	P-Value	Degree of Freedom
Sex								
Female	28	66.36	5.71	68	(61.50 , 71.25)	-0.43	0.66	68
Male	32	68.90	9.57	70	(63.75 , 77.25)			
Total	60	67.95	8.36	68.5	(63.75 , 74.50)			
Age								
20~45years	27	65.15	12.86	67.5	(63.75 , 74.50)	-0.48	0.63	40
Over 46 years	33	68.56	8.52	69.75	(61.25 , 75.25)			
Total	60							

Table 5. Week 8 ISQ and Subject Demographics Analysis

	Number	Average	Standard deviation	Median	(Q1,Q3)	T-Value	P-Value	Degree of Freedom
Sex								
Female	28	70.77	6.25	72	(68.50 , 72.65)	-0.50	0.62	33
Male	32	71.87	6.53	73.5	(69.00 , 76.00)			
Total	60							
Age								
20~45years	27	74.00	4.31	73	(71.25 , 78.63)	1.91	0.06	33
Over 46 years	33	69.91	6.94	71.75	(65.75 , 75.63)			
Total	60							

Table 6. Week 12 ISQ and Subject Demographics Analysis

	Number	Average	Standard deviation	Median	(Q1,Q3)	T-Value	P-Value	Degree of Freedom
Sex								
Female	28	65.85	10.04	69.25	(60.50 , 73.00)	-1.89	0.07	40
Male	32	70.83	7.09	71	(66.63 , 77.00)			
Total	60							
Age								
20~45years	27	70.37	6.97	70	(65.38 , 75.75)	0.87	0.39	37
Over 46 years	33	67.04	9.71	68	(61.00 , 74.00)			
Total	60							

Table 7. Week 16 ISQ and Subject Demographics Analysis

	Number	Average	Standard deviation	Median	(Q1,Q3)	T-Value	P-Value	Degree of Freedom
Sex								
Female	28	76.59	8.73	76.75	(68.88 , 84.00)	1.38	0.18	30
Male	32	72.68	7.29	73	(68.13 , 76.38)			
Total	60							
Age								
20~45years	27	71.31	7.17	73	(66.25 , 73.75)	-2.04	0.05	31
Over 46 years	33	76.98	5.54	76.75	(70.75 , 86.00)			
Total	60							

BMD value of the implant zone during the edentulous period of various subject conditions was analyzed (Table 8). The result showed no statistically significant difference in ISQ in terms of gender and age group ($P > 0.05$). The mean value for the female subjects is 517.50 （±213.52）, while that for the male subjects is 572.06（±205.89）. The mean value for the subjects between 20 to 45 years old is 558.49（±213.52）, while that for the subjects above 46 years old is 572.06（±205.89）.

BMD value of the implantation zone 4 weeks post-surgery (Table 9) indicated no statistically significant difference ($P > 0.05$) in ISQ in terms of gender and age group. The mean value for the female

subjects is 847.14（±219.35）, while that for the male subjects is 821.48（±230.27）. The mean value for the subjects between 20 to 45 years old is 835.55（±234.45）, while that for the subjects above 46 years old is 831.32（±217.20）.

BMD value of the implantation zone 16 weeks post-surgery (Table 10) indicated no statistically significant difference (P > 0.05) in ISQ in terms of gender and age group. The mean value for the female subjects is 829.29（±208.24）, while that for the male subjects is 869.63（±212.22）. The mean value for the subjects between 20 to 45 years old is 858.29（±210.34）, while that for the subjects above 46 years old is 842.85（±211.79）.

Table 8. Pre-surgical Edentulous Zone BMD Analysis

	Number	Average	Standard deviation	Median	(Q1,Q3)	T-Value	P-Value	Degree of Freedom
Sex								
Female	28	517.50	213.52	517.5	(369.9 , 729.8)	-0.61	0.55	58
Male	32	572.06	205.89	568.2	(453 , 709.6)			
Total	60							
Age								
20~45years	27	558.49	213.52	524.3	(394 , 715.6)	-0.25	0.80	58
Over 46 years	33	572.06	205.89	562.5	(437.4 , 740.8)			
Total	60							

Table 9. Post-surgical Edentulous Zone BMD Analysis at Week 4

	Number	Average	Standard deviation	Median	(Q1,Q3)	T-Value	P-Value	Degree of Freedom
Sex								
Female	28	847.14	219.35	912	(630.2 , 1040.5)	0.21	0.84	55
Male	32	821.48	230.27	839.4	(659.5 , 1011.6)			
Total	60							
Age								
20~45years	27	835.55	234.45	890.5	(630.2 , 1046.9)	-0.34	0.74	56
Over 46 years	33	831.32	217.20	872.5	(648.6 , 1025.2)			
Total	60							

Table 10. Post-surgical Edentulous Zone BMD Analysis at Week 16

	Number	Average	Standard deviation	Median	(Q1,Q3)	T-Value	P-Value	Degree of Freedom
Sex								
Female	28	829.29	208.24	891.3	(616.8 , 980)	-0.70	0.49	51
Male	32	869.63	212.22	908.6	(803.2 , 1025.8)			
Total	60							
Age								
20~45years	27	858.29	210.34	908.8	(674.6 , 1040.4)	0.27	0.79	51
Over 46 years	33	842.85	211.79	897.6	(773.3 , 978.2)			
Total	60							

The successfulness of the implantation trial using the Biomate Dental Implants is determined 6 months after the surgery and the installation of the crown; the items considered are listed in Table 11. The results showed that the subjects have reached the criteria for successful implantation.

Table 11. Success and Failure Criteria for Dental Implant

	Success Criteria		Failure Criteria		
Subject No.	Present at the Follow-up Visits	Absent of Implant Movement and Pain	Implant Movement	Bone Resorption Exceeded 1/2 of the	Inflammation of the Surrounding Soft Tissues

				Depth of the Implant in the Alveolar Bone	
No.01	☑	☑	☒	☒	☒
No.02	☑	☑	☒	☒	☒
No.03	☑	☑	☒	☒	☒
No.04	☑	☑	☒	☒	☒
No.05	☑	☑	☒	☒	☒
No.06	☑	☑	☒	☒	☒
No.07	☑	☑	☒	☒	☒
No.08	☑	☑	☒	☒	☒
No.09	☑	☑	☒	☒	☒
No.10	☑	☑	☒	☒	☒
No.11	☑	☑	☒	☒	☒
No.12	☑	☑	☒	☒	☒
No.13	☑	☑	☒	☒	☒
No.14	☑	☑	☒	☒	☒
No.15	☑	☑	☒	☒	☒
No.16	☑	☑	☒	☒	☒
No.17	☑	☑	☒	☒	☒
No.18	☑	☑	☒	☒	☒
No.19	☑	☑	☒	☒	☒
No.20	☑	☑	☒	☒	☒
No.21	☑	☑	☒	☒	☒
No.22	☑	☑	☒	☒	☒
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No.26	☑	☑	☒	☒	☒
No.27	☑	☑	☒	☒	☒
No.28	☑	☑	☒	☒	☒
No.29	☑	☑	☒	☒	☒

No.30	☑	☑	☒	☒	☒
No.31	☑	☑	☒	☒	☒
No.32	☑	☑	☒	☒	☒
No.33	☑	☑	☒	☒	☒
No.34	☑	☑	☒	☒	☒
No.35	☑	☑	☒	☒	☒
No.36	☑	☑	☒	☒	☒
No.37	☑	☑	☒	☒	☒
No.38	☑	☑	☒	☒	☒
No.39	☑	☑	☒	☒	☒
No.40	☑	☑	☒	☒	☒

6. Conclusion

In summary, the trial showed no difference in terms of the successfulness of the implantation between gender and age group. Furthermore, although no statistical significant difference in terms of initial ISQ value was found, it was noted that the mean value of Week 1 ISQ in male subjects is 68.90(±9.57), which is relevantly higher than that of the female subjects at 66.36(±5.71). The mean Week 8 ISQ of male subjects is 71.87(±6.53), which is relevantly higher than that of the female subjects at 70.77(±6.25); the mean value of Week 12 ISQ in male subjects is 70.83(±7.09), which is relevantly higher than that of the female subjects at 65.85(±10.04). The mean of Week 1 BMD value for the male subjects is 847.14(±219.35), which is relevantly higher than that of the female subjects at 821.48(±230.7); the mean of Week 16 BMD value for the male subjects is 869.63(±212.22), which is relevantly higher than that of the female subjects at 829.29(±208.24).

The results of the trial showed that the ISQ of Biomate Dental Implant System increased 5%, 3%, and 9% at Week 8, Week 12, and Week 16, respectively when compared to that of Week 1. BMD value increased 50.57% and 53.27% at Week 4, and Week 16, respectively when compared to that prior to the surgery. In addition, in terms of determine the success of the implant 6 months after the implantation and after the crown installation, every subject has reached the success criteria.

Data from the literature search indicated that the ISQ value for the implant should be greater than 60 at the initial loading. The initial ISQ value measured in the present study is 67.95; in addition, ISQ value taken at Week 8, Week 12, and Week 16, were higher than 60. The finding may serve as a reference in the future for the clinicians to shorten the overall implantation treatment, by determining the appropriate timing to proceed to the next stages of prosthesis placement when the wound has healed completely and the initial ISQ at the implantation site is greater than 60.

7. Filing

The experimental program, protocol, procedures, data, audit report, other relevant documents and final test report are filed and stored at the Research Center for Biomedical Devices and Prototyping Production.

****End of the Report****