Research Paper:

Post-Market Surveillance Study of a Skull Flap Fixation Device: Cranfixer

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ABSTRACT

Background and Aim: Cranfixer was approved in 2017 by the Food and Drug Administration of Iran as a skull flap fixation and also a burr hole cover. The effectiveness and safety of this commercial medical device were investigated in detail by the regulatory auditors.

Methods and Materials/Patients: Cranfixer was used for ninety-five patients. Sixty patients were selected from a list if they had at least two follow-ups after surgery. The following variables were investigated: age, gender, number of Cranfixers, device loosening, infection, and prominence. In addition, a retrospective review was performed about the reason of surgery.

Results: Flap loosening and infection were the major variables surveyed. On average, two Cranfixers were used for each patient. Patients' median age was 44 years. There was no sex preference (50% male). The craniotomy occurred in frontal (50%), occipital (3%), parietal (20%), and temporal (27%) lobes. Based on examination and CT imaging, no cases of loosening were observed. Just in one patient, one of two Cranfixers was infected (P<0.001).

Conclusion: The reliability and functionality of Cranfixer were proved in pre-market test and the results of this study confirm them. Cranfixer provides safe, reliable and long-term functionality.

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Highlights

- The reliability and functionality of Cranfixer is studied based on the clinical data.
- Cranfixer provides safe, reliable and long-term functionality.
- The thickness of Cranfixer should be revised without loss of strength and product performance.

Plain Language Summary

The cranfixer is a medical device in neurosurgery field manufactured by Darman Afarin Noandish Afagh co (DanaWell). The most remarkable outcome of this study is the functionality of Cranfixer. Cranfixer is a skull flap fixation and also a burr hole cover. The clinical investigation lasted up to 18 months. This device was approved in 2017 by the Food and Drug Administration of Iran.

1. Introduction

Craniotomy is a common surgical procedure in neurosurgery. After craniotomy, the removed piece of bone must be returned. Various fixation techniques are used for securing the bone in place. These techniques vary from making holes in the bone and simple suturing to fixation with the biocompatible implantable fixators.

Suturing technique is a basic method in which a stainless steel wire is used to secure the fixation [1]. Holes are drilled in the flap and the adjacent bone which are twisted with a wire that passes through the holes. In addition, the strips are used to fix skull flaps in place with screws [2].

The most novel technique is clamping the flap. The clamping method is simple to use and reduces the surgery time. Clamps are made of different materials such as titanium and PEEK [3, 4]. Cranfixer is made of Poly-Methyl Methacrylate (PMMA), a well-known long-term biocompatible material that has long been used [5, 6]. Cranfixer was approved by Iran's Ministry of Health and Medical Education after qualification review and related standard audition for biocompatibility, mechanical strength, and easy handling. We examined and reported surgeon experience and patient satisfaction in the present study. Cranfixer is fixed with silk sutures as shown in Figure 1. This is an easy and applicable mechanism. In Figure 2, a flap fixation is shown with two Cranfixers.

2. Methods and Materials/Patients

Sixty patients who had at least two follow-ups were included in this study. The main cause of surgery was brain tumors. Patients' age ranged from 14 to 82 years (mean age=44). There were equal numbers of male and female. Cranfixer was used in different parts of the skull as shown in Figure 3.

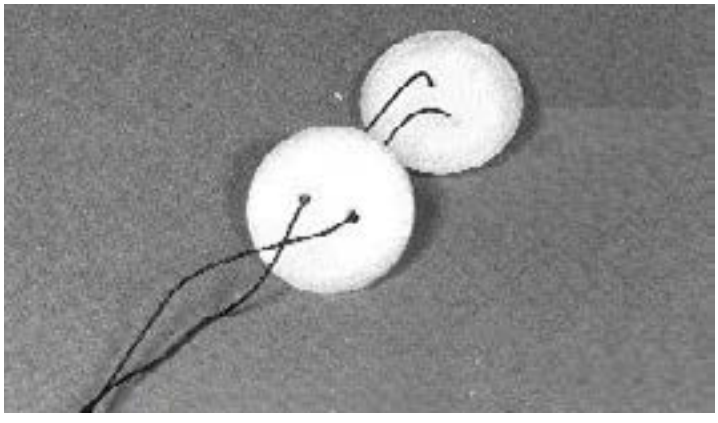

Figure 1. Cranfixer

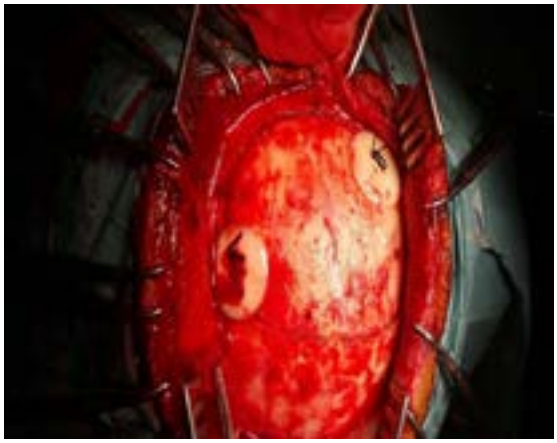

Figure 2. Flap fixation with Cranfixer

Different measures were chosen to evaluate infection, device loosening and prominence through scalp (both visual and touch) from surgeons' and patients' perspective. Follow-ups ranged from 143 to 523 days with a mean follow-up of 342 days. Pearson's chi-square method was used for statistical analysis.

Characteristics and demographics of the participants were summarized with descriptive statistics. Patients were referred for therapy and selected from the age range of 14 to 82 years old, consisting of males and females. It was not possible to blind the surgeons because they were familiar with Cranfixer. Clinical Research Form/Case Report Form (CRF) was developed according to the guidelines of FDA of Iran and CONSORT statement.

The first part of this study obtained data from the surgeon's experience at the time of surgery. The second part of data was collected from patient follow-ups in two rounds. Comorbidities like immunodeficiency were not observed in these follow-ups.

Cranfixers were used in frontal, temporal, parietal and occipital regions of the skull. Complications such as infection, loosening, visual prominence and tactile prominence were included in statistical analysis. According to the surgical history, patients were followed up 143 to 523 days to assess the instances listed. Pearson's chi-square was used for statistical analysis.

In accordance with the ethical principles and the national norms and standards for conducting medical research in Iran, the questionnaire and method of this study were evaluated and approved by the Research Deputy of Tehran University of Medical Sciences (IR.TUMS.VCR.REC.1397.657)

3. Results

As mentioned before, patients with at least two followups are reported in this study. Figure 4 shows the implanted Cranfixers in some postoperative images.

Table 1 presents patient demographics: gender, age, follow-up duration, number of Cranfixers used, size of bone flap, location of bone flap in the skull, patient's disease, flap loosening, infection and prominence (visual/tactile). In the following, the variables and the data are presented in tables and charts. The variables are: 1) gen-

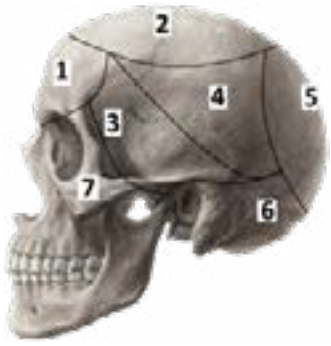

Figure 3. skull segmentation

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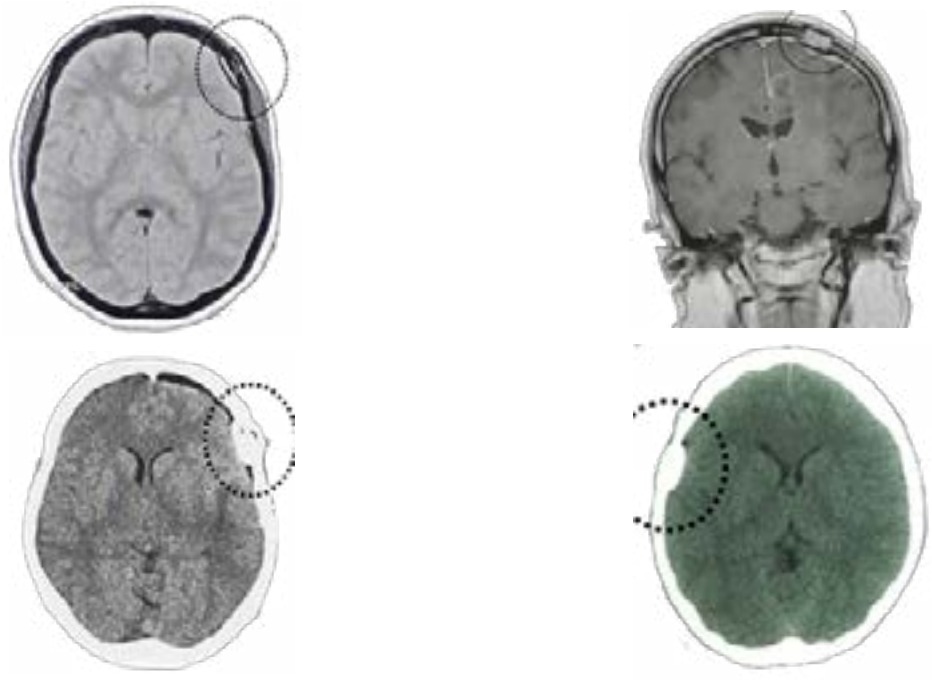

Figure 4. Cranfixers in postoperative images of different patients

der, 2) age, 3) duration of the follow-up, 4) number of Cranfixers used for each patient, 5) flap size, 6) location of defect on the skull, 7) disease, 8) flap loosening, 9) infection, and 10) prominence (visual/tactile) (Table 1). The quantitative variables are described in Table 2. The mean age of patients was 44 years old (ranged: 14-82).

Another important quantitative variable is the follow-up duration. Among 95 patients, 60 individuals were selected with at least two follow-ups. The mean follow-up duration was 342 days while the longest duration of 525 days belonged to a 14-year-old girl. In most surgeries, two Cranfixers were used for each patient. Totally, 118 Cranfixers were implanted in 60 patients.

Table 3 presents some variables about the surgery. Most of the dissection flaps were large (80%) and located on frontal (50%) region. After the frontal region, the temporal and parietal regions were ranked second and third, respectively, in frequent surgical sites. Tumor was the most prevalent cause of surgery in this study (88%). The relationships of craniotomy location with flap size and diseases are shown in Table 4. In most cases, large flaps were in frontal region. We considered flap size of >16 mm^2 as large. Chi-square was used to assess statistical significance of different variables. The calculated P-value proves the significance of these relationships (Table 5).

Finally, the most important variables, the objectives of this study, are presented in Table 6. Totally, there was no evidence of loosening. Infection was reported only in one case (1.7%). The cause of infection was investigated thorough product tracking form and the LOT number. Two Cranfixers were used for the infected case with same LOT number and sterilization date. The documentation and standard indicators show that both of these Cranfixers were sterilized in a standard manner, but only one of them was infected. As a result, based on these pieces of evidence, the probability that the infection had been caused by the product is very slight (P<0.001). The responsible surgeon believed the silk stitch may have caused the infection.

Another important characteristic of Cranfixer is prominence after surgery. In five cases, the Cranfixer was touchable through scalp (8.3%) and just three of them were visible if carefully inspected (5%). This characteristic is not usually of clinical importance, but it may compromise patient's appearance and self-confidence. Therefore, it must be considered in future versions of Cranfixer.

4. Discussion

This study supports previous studies regarding biocompatibility of PMMA. Cranfixer revealed good performance regarding flap fixation and was easy to use

Table 1. The datasheet of variables

No	Patient Code	Gender	Age	Duration FU	No.	Falp Size	Craniotomy Site	Disease	Loosening	Infection	Prominence (Vision)	Prominence (Touch)
1	8547	Female	48	219	2	Small	Temporal	Tumor	No	No	No	No
2	16403	Female	56	143	1	Small	Temporal	Tumor	No	No	No	No
3	22040	Female	52	188	2	Large	Temporal	Tumor	No	No	No	No
4	24445	Male	45	182	1	Small	Parietal	Tumor	No	No	No	No
5	25394	Male	33	343	2	Large	Frontal	Tumor	No	No	No	Yes
6	25718	Male	30	381	2	Large	Temporal	Seizure	No	No	No	No
7	25904	Female	31	375	2	Large	Frontal	Tumor	No	No	No	No
8	26426	Female	36	371	2	Large	Frontal	Tumor	No	No	No	No
9	26695	Male	71	501	2	Large	Frontal	Tumor	No	No	No	No
10	26777	Male	60	269	2	Large	Frontal	Tumor	No	No	Yes	Yes
11	26934	Female	37	465	2	Large	Frontal	Tumor	No	No	Yes	Yes
12	26992	Female	14	525	2	Small	Parietal	Seizure	No	No	No	No
13	27060	Female	49	315	2	Large	Frontal	Tumor	No	No	Yes	Yes
14	27165	Male	66	523	2	Large	Frontal	Tumor	No	No	No	Yes
15	27202	Female	26	518	2	Large	Frontal	Tumor	No	No	No	No
16	27246	Female	46	444	2	Large	Frontal	Tumor	No	No	No	No
17	27255	Male	48	493	2	Large	Frontal	Tumor	No	No	No	No
18	27273	Female	33	480	2	Small	Temporal	Tumor	No	No	No	No
19	27308	Male	64	479	2	Large	Occipital	Tumor	No	No	No	No
20	27323	Male	51	516	2	Large	Parietal	Tumor	No	No	No	No
21	27339	Female	81	456	2	Large	Frontal	Tumor	No	No	No	No
22	27346	Male	33	448	2	Large	Frontal	Tumor	No	No	No	No
23	27352	Male	46	451	2	Small	Temporal	Seizure	No	No	No	No
24	27367	Female	32	471	2	Large	Frontal	Tumor	No	No	No	No
25	27392	Male	36	467	2	Large	Frontal	Tumor	No	No	No	No
26	27407	Female	50	453	2	Large	Parietal	Tumor	No	No	No	No
27	27426	Female	35	430	2	Large	Frontal	Tumor	No	No	No	No
28	27435	Male	82	447	2	Large	Frontal	Tumor	No	No	No	No
29	27455	Male	64	441	2	Large	Parietal	Tumor	No	No	No	No
30	27460	Male	37	439	2	Large	Frontal	Tumor	No	No	No	No
31	27511	Male	15	425	2	Large	Occipital	Tumor	No	No	No	No
32	27512	Male	22	427	2	Small	Parietal	Tumor	No	Yes	No	No
33	27594	Female	29	378	2	Large	Frontal	Tumor	No	No	No	No
34	27612	Female	56	360	2	Large	Frontal	Tumor	No	No	No	No
35	27629	Male	35	365	2	Large	Parietal	Tumor	No	No	No	No
36	27650	Male	33	368	2	Small	Temporal	Tumor	No	No	No	No
37	27662	Male	64	353	2	Large	Frontal	Tumor	No	No	No	No
38	27676	Male	54	397	2	Large	Temporal	Tumor	No	No	No	No
39	27694	Male	41	346	2	Large	Frontal	Tumor	No	No	No	No
40	27716	Male	19	266	2	Small	Parietal	Seizure	No	No	No	No

No	Patient Code	Gender	Age	Duration FU	No.	Falp Size	Craniotomy Site	Disease	Loosening	Infection	Prominence (Vision)	Prominence (Touch)
41	27761	Male	58	322	2	Large	Parietal	Tumor	No	No	No	No
42	27766	Female	53	327	2	Large	Frontal	Tumor	No	No	No	No
43	27771	Female	38	307	2	Small	Temporal	Seizure	No	No	No	No
44	27857	Male	68	302	2	Large	Temporal	Tumor	No	No	No	No
45	27870	Female	52	288	2	Large	Frontal	Tumor	No	No	No	No
46	27880	Male	38	301	2	Large	Frontal	Tumor	No	No	No	No
47	27985	Female	17	168	2	Small	Temporal	Seizure	No	No	No	No
48	28021	Male	21	274	2	Large	Temporal	Tumor	No	No	No	No
49	28040	Female	50	171	2	Large	Parietal	Tumor	No	No	No	No
50	28045	Male	15	215	2	Small	Temporal	Seizure	No	No	No	No
51	28071	Female	45	235	2	Large	Parietal	Tumor	No	No	No	No
52	28076	Female	55	230	2	Large	Frontal	Tumor	No	No	No	No
53	28097	Male	57	222	2	Large	Temporal	Tumor	No	No	No	No
54	28141	Female	25	194	2	Large	Frontal	Tumor	No	No	No	No
55	28243	Female	69	211	2	Large	Temporal	Tumor	No	No	No	No
56	28256	Female	59	208	2	Large	Parietal	Tumor	No	No	No	No
57	28330	Male	40	165	2	Large	Frontal	Tumor	No	No	No	No
58	28306	Female	62	157	2	Large	Frontal	Tumor	No	No	No	No
59	28326	Female	30	154	2	Large	Temporal	Tumor	No	No	No	No
60	28394	Female	37	161	2	Large	Frontal	Tumor	No	No	No	No

Table 2. Age, follow-up duration, and number of Cranfixers per patient

Variables	Min	Max	Mean±SD
Age	14	82	44.15±16.51
Follow- up duration (day)	143	525	342.17±117.49
Number of Cranfixers per patient	1	2	1.98±1.81

Table 3. Some variables related to the surgery

Variables	Type	Frequency	(%)
Flap size	Large	48	80
	Small	12	20
Craniotomy site	Frontal	30	50
	Occipital	2	3
	Parietal	12	20
	Temporal	16	27
Disease	Seizure	7	12
	Tumor	53	88

Table 4. The frequency of flap size and disease in each craniotomy location

Description		Frontal	Occipital	Parietal	Temporal
Flap size	Large	30	2	8	8
	Small	0	0	4	8
Disease	Seizure	0	0	2	5
	Tumor	30	2	10	11

Table 5. The results of chi-square test

Description		value	df	P
Relationship between flap size and craniotomy site	Pearson's chi-square	18.33	3	0.000
	Likelihood ratio	22.60	3	0.000
	Number of valid cases	60	-	-
Relationship between disease and craniotomy site	Pearson chi-square	10.47	3	0.015
	Likelihood ratio	12.54	3	0.006
	Number of valid cases	60		

Table 6. The clinical variables

Variables		Frequency	(%)
Loosening	No.	60	100
	Yes	0	0
	Total	60	100
Infection	No.	59	98.3
	Yes	1	1.7
	Total	60	100
Prominent (visual)	No.	57	95
	Yes	3	5
	Total	60	100
Prominent (tactile)	No.	55	91.7
	Yes	5	8.3
	Total	60	100

according to the surgeon. Thickness of the device is a point for further revision and development.

Our clinical investigation lasted up to 18 months, and we observed the following characteristics of Cranfixer: 1. Good performance in the flap fixation; 2. Excellent biocompatibility; 3. user-friendliness and ease to use from the surgeons' point of view. Furthermore, the thickness of Cranfixer should be revised without loss of strength and product performance.

Ethical Considerations

Compliance with ethical guidelines

The Case Report Form (CRF) and informed consent of this study were designed and used according to the approved procedure of Food and Drug Administration of Iran. The questionnaire and method of this study were evaluated and approved by the Research Deputy of Tehran University of Medical Sciences (IR.TUMS.VCR.REC.1397.657).

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Authors contributions

Conceiving and designing the study: Seyed Roholah Ghodsi, Zahra Namazi; Data collection and manuscript drafting: Hosein Esmaili Dezaki, Zahra Faraji; Data collection and statistical analysis: Morteza Alizadeh, Hosein Esmaili Dezaki; Study design and analyses; Seyed Roholah Ghodsi, Zahra Namazi, Morteza Alizadeh

Conflict of interest

The authors with DanaWell affiliation have indirect financial interest in the subject matter discussed in this paper.

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