# CASTomize Pilot Study Protocol

Principle investigator: Dr Michael Yam

Co-investigator: Dr Trevor Binedell, Dr Bernice Heng

Industrial collaborator: Abel Teo, Eleora Teo, Johannes Sunarko

# CASTomize pilot study protocol: a randomized controlled trial comparing CASTomize 4D printed cast versus standard of care fiberglass cast on fracture reduction and patient reported outcomes.

**Abstract**

**Background:** For many years, traditional fibreglass casting has been the gold standard of immobilisation for distal radius fractures (DRFs). However, the traditional method of casting has obvious disadvantages such as poor patient comfort, inability to be in contact with water, difficulty observing skin underneath and requiring multiple cast changes in the patients care journey. This study compares the Castomize 4D printed casts versus the conventional fiberglass cast in fracture immobilisation, and various patient reported outcomes.

**Methods/design:** This study is a randomised control trial comparing Castomize 4D printed cast versus conventional fibreglass casts in isolated conservatively treated distal radius fractures. The primary outcome measure is fracture reduction. Secondary outcome measures include patient reported outcome measures such as the Adult Rated Cast Evaluation Questionnaire (ARCEQ)[1][2], comfort of the cast, quality of life assessed with the EQ-5D-5L questionnaire[3], cost-effectiveness and adverse events occurrence. In total, 30 patients will be included and followed for 6 months.

**Trial registration:** Pending

**Registration number:** Pending

## Background

Displaced distal radius fractures (DRF) are very common in the adult population and their incidence is still on rising trend due to aging population. This is an issue which is pervasive across all ages, but most common in the elderly. In 2019, 180 million fractures happened worldwide. An average of 5 fracture incidents occurs every second. The current gold standard in fracture immobilisation is via the application of a fibreglass cast. However, the current fibreglass cast has multiple disadvantages. The cast is bulky, has poor ventilation and cannot come into contact with water. This gives patients considerable discomfort, and are unable to bathe and provide hygiene to their injured limb for the duration of the casting. Because the cast is not breathable, skin maceration, itchiness and wounds

may become an issue. In this light, multiple casts changes become necessary to reduce the risk of soft tissue complications and to provide patient comfort. This increases the wastage of materials for the fibreglass casting as well as increases healthcare burden for the cast changes.

Castomize has created a 4D printed cast with its proprietary materials and designs aimed at overcoming the challenges in the traditional casting methods. Its 4D printed casts are lightweight and breathable, allowing contact with water and hygiene. Its design facilitates visualisation of the skin and soft tissue conditions. It is also remouldable, potentially only requiring one device for the duration of the patients care journey.

The design of the 4D printed cast was done in collaboration with orthopaedic clinicians, prosthetists and senior casting technicians optimised for clinical use. A biomechanical test was performed to evaluate the biomechanical properties of the 4D printed cast in comparison to the conventional fibreglass casts and were found to be less stiff and with a lower load to failure. This was however accessed to be not clinically significant.

Therefore, this study aims to compares the Castomize 4D printed casts versus the conventional fiberglass cast in fracture immobilisation and various patient reported outcomes.

## Methods/design

This manuscript is written according to the Consolidated Standards for Reporting Trials (CONSORT statement) and Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT guidelines).

### Objectives

The primary aim of the study is to assess non inferiority of the Castomize 4D printed cast versus conventional fibreglass casts in fracture immobilisation and reduction.

The secondary aim of the study is to assess differences in patient reported outcomes measures (ARCEQ, comfort of the cast, EQ-5D-5L, cost-effectiveness and adverse events occurrence) in the Castomize 4D printed cast versus conventional fibreglass casts.

### Design, participants, interventions and outcomes

*Study design and randomization*

A randomised controlled trial will be conducted in a single institution: TTSH.

Patients will be recruited at the outpatient clinic. Patients who meet the inclusion and exclusion criteria will be recruited and randomised into 2 groups. Randomisation will be carried out via block randomisation via a computer generated randomization sequence.

Group 1: Castomize 4D printed cast (Figure 2)

Patients randomized to group 1 will undergo fracture immobilisation with the Castomize 4D printed cast via the care team (Casting technician/ clinical team). The Castomize 4D printed cast is appropriately heated and then moulded to the patients wrist as per usual manipulation and reduction techniques. The cast is held in position until hardened.

Group 2: Conventional casting (Figure 1)

Patients randomized to group 2 undergo fibreglass casting as per the standard of care.

In both groups, post casting X-rays are taken to assure fracture reduction and recasting may be attempted in the event of inadequate fracture reduction.

A patient information sheet will be provided to the patient explaining the study protocol, and what to look out for in caring for their casts.

**Inclusion criteria**
– Age ≥ 21 years
– Distal radius fracture for conservative treatment within 3 weeks of initial injury

**Exclusion criteria**
– Concomitant injuries to the ipsilateral extremity, interfering with the treatment of the DRF (Example: concomitant elbow fracture that requires further immobilisation with a above elbow cast)
– Inability to complete study forms due to any cognitive, mental issues.
– Pregnant women

*Study procedures and timeline*
Measurements will take place at 6 time points as shown in Table 1. These time points are baseline (T0), 1 week (T1), 2 weeks (T2), 6 weeks (T3), 3 months (T4) and 6 months (T5) after inclusion in the study. At T0, baseline characteristics will be gathered. An inclusion form will be filled in by the treating physician providing fracture and treatment-specific information. Second, patients receive a questionnaire, providing predominantly patient and injury-specific information. The list of baseline characteristics is shown in Table 2. Patients receive questionnaires at T1 to T5. These questionnaires are carried out by phone call. Posterior-anterior (PA) and lateral radiographs of the wrist will be taken at T0 (before and after reduction) and during follow-up at T1 –T4 as per standard of care. Physical examination of the wrist will take place at T4 and will be performed by the research team.Study visit may be administered via phone call. Functional tests will be performed at patient earliest appointment.

**Table 1** Schedule of activities

| | T0<br>Baseline | T1<br>D7±3 | T2<br>D14 ±3 | T3<br>D35 ± 7 | T4<br>D84 ±14 | T5<br>D168 ±21 |
|---|---|---|---|---|---|---|
| Inclusion form | √ | | | | | |
| X-rays* | √ | √ | √ | √ | √ | |
| Functional tests** | | | | | √ | √ |
| VAS | | √ | √ | √ | √ | √ |
| Photograph | | √ | | | | |
| Comfort of cast | | √ | √ | √ | | |
| Analgesic use | | √ | √ | √ | √ | √ |
| EQ 5D5L | | √*** | | √ | √ | √ |
| ARCEQ | | | | √ | √ | √ |
| MCQ- iMTA | | | | √ | √ | √ |

| | | | | | | |
|---|---|---|---|---|---|---|
| PCQ- iMTA | | | | √ | √ | √ |
| | | | | | | |

*X-rays before and after reduction (obtained from standard of care results if available)
**ROM, grip strength done by study team. ROM, DRUJ and Kapandji will be collected as part of standard of care if available
*** EQ 5D5L status pre-fracture and post-fracture sustainment

**Table 2** Baseline characteristics

| **Baseline characteristics** | |
|---|---|
| Date of emergency room visit | Sex |
| Affected wrist | Date of Birth |
| Method of reduction | |
| | Hand dominance |
| | Mechanisms of injury |
| | Smoking Status |
| | General medical history |
| | Previous injuries of the affected extremity |
| | La Fontaine criteria |

*Outcome*

**Primary outcome** The primary outcome of this study is the occurrence of fracture displacement assessed on PA and lateral radiographs at 1, 2 and 6 weeks. Displacement of the radius is defined by: As compared to the post reduction radiograph at T0, Displacement of : > 15° of dorsal angulation, > 20° of volar angulation, < 15° of radial inclination, > 3mm of radial shortening and > 2mm intraarticular
step-off or gap. Measurements will be on standard PA and lateral radiographs of the wrist by trained members of the research team.

**Secondary outcomes** An overview of measurements is shown in Table 1.

- Comfort of the cast assessed via pictorial representation of pressure marks or areas of discomfort.
- Severity of pain evaluated with the Visual analogue Score (VAS)
- Patient will describe their average wrist symptoms over the past week on a scale of 0-10 using Adult Rated Cast Evaluation Questionnaire (ARCEQ) [6][7].
- Quality of life will be assessed using the 5-level EuroQol (EQ-5D-5L) scoring questionnaire.
- Cost-effectiveness will be measured using the Medical Consumption Questionnaire (iMCQ) and the Production Consumption Questionnaire (iPCQ) [8].
- Physical examination:
    - Range of motion (ROM) of the wrist will be measured with a goniometer. ROM concerns dorsal flexion, volar flexion, radial deviation, ulnar deviation, pronation and supination.
    - Grip strength will be measured with a Jamar hydraulic hand dynamometer. The maximum score for each side over 3 attempts will be used
    - Specific testing of the wrist and hand will be performed namely:
        - distal radioulnar joint (DRUJ) stability tested with the DRUJ ballottement test

        - opposition of the thumb using the Kapandji score
        - finger stiffness will be measured with finger-to-palm distance, tested from the tip of the finger to the distal palmar crease when the fingers are in maximal active flexion

    ROM and grip strength on the injured side will be compared with the uninjured side.
- Number of conversions to surgical treatment and other (serious) adverse events will be monitored. (Eg: Skin complications)

It is expected that a proportion of patients will fail conservative treatment with displacement of the distal radius fracture at week 1 or week 2 follow up. These patients will continue with surgical fixation of their fractures and no further trial procedures will be required.

*Adverse events reporting*
All adverse events reported by the patient or observed by the treating physician or researcher will be recorded. Serious adverse events (SAE) will be reported to the Domain Specific Review Board (DSRB), which approved the protocol.

Serious adverse events are defined as:
– Skin related problems requiring surgical intervention (Eg: Ulcer, infection, necrosis)
- Compartment syndrome
- Cast related injury to the patient resulting in loss of limb or life

Study related serious adverse events are defined as:
– Compartment syndrome

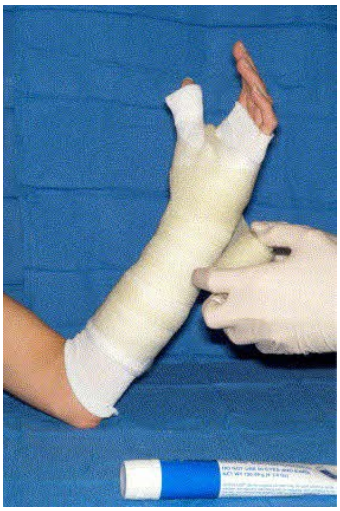

*Fig 1 Conventional Fiberglass cast[9]*

*Fig 2 CASTomize 4D printed cast*

**Data analysis**

General descriptive statistics will be performed on baseline patient and fracture characteristics. Patients will be analysed according to the intention-to-treat principle.

*Primary outcome*

The primary outcome, fracture re-displacement, will be analysed using a mixed-effects logistic regression. To account for clustering, a random intercept for the hospitals will be used. Fixed effects will be the covariates we adjust for as reported in the literature, namely age, presence of osteoporosis, and fracture characteristics. If new prognostic factors will be identified and reported in the literature, these factors will also be added as covariates.

*Secondary outcomes*

For secondary outcomes, trends between baseline and follow-up time points (T0-T5) will be assessed using linear mixed models for repeated measures. This accounts for comfort of the cast, recovery of function and grip strength, pain severity (VAS), ARCEQ and EQ-5D-5L scores. The number of conversions to surgical fixation and complications will be determined using Fisher Exact or Chi-square test, depending on the magnitude of results.

*Cost-effectiveness analysis*

Both cost-effectiveness (CEA) and cost-utility (CUA) analysis will be performed from a societal perspective. For the calculation of medical costs, we will use charges as published in Singapore guidelines as a proxy of real costs. The unit per price of the cast application in patients with DRF will be calculated with the microcosting method. Intramural costs (i.a. additional diagnostics, number of hospital visits, in case of hospital admission the length of stay etc.) are collected from the electronic health record. Productivity costs will be registered in detail by the iPCQ. The iMCQ and the iPCQ are validated by the Institute of Medical Technology Assessment (Erasmus University, Rotterdam, The Netherlands).

The difference in costs and effects of CASTomize instead of a circumferential cast will be calculated as incremental cost-effectiveness ratio (ICER). The primary effect outcome measures will be the number of re-displacements for the CEA and quality-adjusted life years (QALY) for the CUA. QALYs will be measured, based on the Singaporean tariff for the EQ-5D-5L.

The sensitivity analysis will assess the robustness of the results to changes in costs and effect parameters. Bootstrapping with 1000 replications will be used to estimate 95% confidence intervals around cost differences and the uncertainty surrounding the ICERs. This will be graphically presented on cost-effectiveness planes and acceptability curves using the net benefit framework. For the time horizon of 6 months, discounting is not necessary.

**Data management**

All data are handled confidentially and anonymized in compliance with the Singapore Personal Data Protection Act (PDPA). Personal data of participants will be changed by a study number. This number is used for all study documentation, study reports and publications. The key of this study number will be handled by an independent researcher. During the study period, all data will be collected and managed using GemsTracker electronic data capture tools. Paper case report forms are entered in GemsTracker by the researcher and the original paper case forms will be filed in the investigator site file at the recruiting hospital. All data is stored for 10 years.

*Data monitoring*

Since the study is labelled as low risk, a data safety monitoring board is not required.

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