# Secrets in scaphoid fractures

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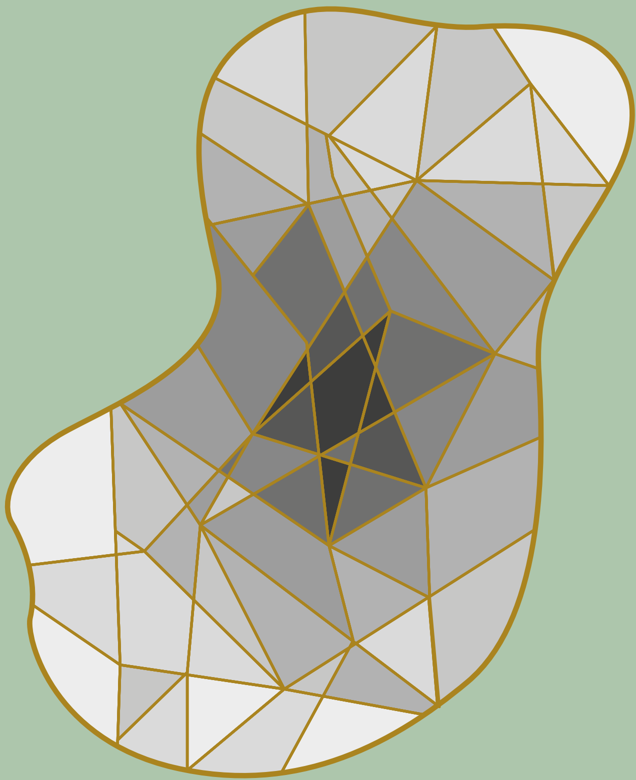
# Secrets in Scaphoid Fractures



Tessa Drijkoningen

Secrets in

# Scaphoid fractures

Tessa Drijkoningen

This PhD thesis was embedded within Amsterdam Movement Sciences research institute, at the Department of Plastic and reconstructive surgery, University of Amsterdam, the Netherlands.

Colophon



This thesis was prepared at the Orthopaedic Hand and Upper Extremity Service Massachusetts General Hospital, Harvard Medical School, Boston, MA, United States of America, and the Plastic, Reconstructive and Hand Surgery Department, Amsterdam University Location Academical Medical Center, University of Amsterdam, The Netherlands

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# Secrets in

# Scaphoid fractures

ACADEMISCH PROEFSCHRIFT

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aan de Universiteit van Amsterdam
op gezag van de Rector Magnificus
prof. dr. ir. K.I.J. Maex
ten overstaan van een door het College voor Promoties ingestelde commissie,
in het openbaar te verdedigen in de Agnietenkapel
op vrijdag 1 maart 2019, te 14:00 uur
door Tessa Drijkoningen
geboren te Cambridge

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Faculteit der Geneeskunde

Aan mijn ouders

You can tell a woman's age by her hands (Jesse J Jupiter)

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# PART I

## GENERAL INTRODUCTION

ARBURY
Kings Hedges Rd
Arbury Rd
Milton Rd
Huntingdon Rd
Gilbert Rd
B1049
A1134
High St
A1134
Chesterton Rd
A1303
Bridge of Sighs
Travelodge
Newmarket
Cambridge
A1134
Coldhams Ln
The Fitzwilliam Museum
A603
A603
Cambridge
University
Botanic
Garden
Grantchester Rd
Coleridge Rd
A1134
A1134
A1307
Cherry Hinton Rd
A1134
rantchester
A1134
A1134
Queen E
High St
Addenbrooke's Hospital

# Chapter I

## Introduction

# Introduction

Scaphoid fractures were first described in 1905 by Destot, a French pioneer in analyzing wrist problems just after the discovery of radiography of the wrist.[1] In 1896 the first radiographs of the wrist were described by Roentgen, it might have been in 1890 in Maastricht which has never been published.[2] The French pioneer Destot in combined studying wrist anatomy, radiographic interpretations and clinical conditions which lead to a classification of various carpal injuries including a classification for scaphoid fractures.[1] Shortly after, scaphoid fractures became notorious for their troublesome healing. In an early review of 1939, Cravener tried to clarify factors contributing to the establishment of nonunion. He encouraged dividing scaphoid fractures to age and location. *"In discussing carpal scaphoid fractures, we must first arrive on a common ground. Is the fracture through the tuberosity, the waist, or the body? If it is through the tuberosity we can practically neglect it, for it will hea1. If it is through the body it will not easily heal.*[3] The scaphoid is the most important bone regarding wrist functionality and fractures are infamous because of troublesome healing. It is notorious how a common fracture of this bone is infamous, even though it represents 2-7% , and is one of the greatest challenges to all physicians involved in trauma care.[4,5] Non-uniting scaphoid fractures often progress to a degenerative collapse of the carpal bones in the wrist, requiring a complex salvage procedure such as a proximal row carpectomy or a four corner arthrodesis, resulting in wrist stiffness.[6,7] Due to these reasons, an extremely careful approach is adopted. The myth that all scaphoid fractures require months (8-12 weeks) of cast immobilization in order to heal, is leading to the fact that a lot of patients will probably be over-treated.[8]

# Current Issues

## Aims of this Thesis

*Firstly*, the aim is to clarify current issues in classifying scaphoid fractures and to find a simplified classifying-system using 3D techniques. *Secondly*, to improve the knowledge on important fracture features, and especially differences in interpretation of diagnostics used for scaphoid fractures. *Thirdly*, the aim is, now that we understand what the current issues are, to have a sneak preview into possible future diagnostics.

## Outline of this Thesis

This thesis is structured to address the current status in classifying, diagnosing and future diagnostics in scaphoid fractures. In order to improve understanding and differences in interpretation of diagnostics worldwide we need to better understand fracture patterns and factors adding to long term clinical outcome.

# 1. CLASSIFYING SCAPHOID FRACTURES

Classifications of Acute Scaphoid Fractures: A Systematic Literature Review

Over the last few decades, several classification systems and imaging technologies have been proposed for the diagnosis of scaphoid fractures in order to improve prediction of healing and select optimal treatment ranging from cast immobilization to internal fixation. Currently, the Russe, Mayo, and Herbert systems are commonly used in clinical practice.[9,10,11] These classifications are based on fracture planes, fracture location and stability, respectively.

Primary aim;

To find the reliability of existing classification systems for scaphoid fractures and to test reproducibility.

A 'simplified classification' in scaphoid fractures; Part 1 and Part 2

Identifying specific scaphoid fracture patterns might change treatment choices as outcomes can become more predictable. Currently three-dimensional models can be derived directly from CT-scans using a computer. Three main groups of fractures could be identified: (1) proximal pole fractures (proximal to the distal scapholunate (SL) interval), (2) a range of waist fractures (involving the scaphocapitate (SC) interval), and (3) distal tubercle fractures (involving the STT interval).

Primary aims for these two studies;

- To distinguish the various clusters of acute scaphoid fracture patterns using 3D models.
- To analyze the relative volume of fracture fragments and identifying any shared common fracture area.
- To test the found simplified classification using a large database of scaphoid fractures diagnosed on posteroanterior radiographs.
- An additional inter-observer study compared this simplified classification with the Herbert classification

# 2. PHYSICIAN INTERPRETATION OF DIAGNOSTICS

Interobserver variability in diagnosis of scaphoid proximal pole fractures

Fractures of the proximal pole of the scaphoid are prone to adverse outcomes, such as nonunion and avascular necrosis.[7,8,12,13] Operative treatment is more readily considered for proximal pole fractures than for waist fractures.[14] The data regarding the management of proximal pole fractures may be clouded by imprecision in distinction of waist fractures from proximal pole fractures.

Primary aim;
We studied the interobserver agreement for the diagnosis of proximal pole fractures of the scaphoid between observers that view radiographs alone and those that review radiographs and CT scans. It also addresses the secondary aim to identify fracture displacement.

Reliability of Diagnosis of Partial Union of Scaphoid Waist Fractures on Computed Tomography
Scaphoid waist fractures can result in non-union. Radiographs are often used to diagnose union and some surgeons may prolong cast immobilization based on radiographic findings. The study of Dias and colleagues demonstrated that radiographs are not reliable for diagnosis of union.[15] Computed tomography is increasingly used not just to diagnose union, but also to estimate the percentage of the fracture gap that is bridged by healing bone. Moreover, the concept of percent union on CT scans is often used in studies of scaphoid waist fractures.
Primary aim;
This study tested the agreement between observers on the extent of union of a scaphoid waist fracture on computed tomography.

Plain radiographs are reliable in distinction of nonunions from acute fractures of the scaphoid waist without computed tomography
Some patients that present with wrist pain after a fall have an old scaphoid nonunion they may not have been aware of. Some *active* patients (e.g. athletes) may have had several recent falls, so the fracture detected may have occurred weeks, months, or years prior. After a fall, a patient with an established scaphoid nonunion or with or without associated arthritis may relate the problem to a recent event. These misconceptions might bias clinicians to misinterpret nonunions as acute fractures, with the potential for undertreatment (e.g. percutaneous screw fixation when debridement and bone grafting of the nonunion is needed). Computed tomography (CT) might help distinguish acute fractures from nonunions.
Primary aim;
We studied the agreement between observers on distinction of acute scaphoid waist fractures from nonunions using only radiography compared to radiography and a CT-scan. We also evaluated the physician factors associated with better agreement and the confidence of the observers.

## 3. FUTURE DIAGNOSTICS

Inter-observer agreement between 2-dimensional versus 3-dimensional I-Space model in the diagnosis of occult scaphoid fractures

To date no consensus regarding different diagnostic modalities in diagnosing scaphoid fractures has shown to be the gold standard (2). An example of a new form of diagnostic modality is the I-Space; a CAVE-like virtual reality system. A "hologram" of a 3D modality dataset is visualized as a floating image in front of the viewers. The viewers wear a pair of glasses with polarizing lenses that allow the bony structures to be seen as free-floating objects in three dimensions.

Primary aim;

To get pilot data on the diagnostic value of the I-Space in detecting occult scaphoid fractures.

## References


1. Peltier LF. The classic. Injuries of the wrist. A radiological study. By Etienne Destot. 1926. Clin Orthop Relat Res. 1986(202):3-11
2. K Spiegel, The first clinical X-ray made in America-100 years, AJR 1995 164;241-243.
3. Cravener EK, McElroy DG. Fractures of the Carpal (Navicular) Scaphoid. American Journal of Surgery. 1939;44(1):8
4. Beeres FJ et al. Scaphoid fractures: diagnosis and therapy. Ned Tijdschr Geneeskd 2007;151-13:742-7
5. vd Molen AB et al. Time off work due to scaphoid fractures and other carpal injuries in The Netherlands from 1990 to 1993. J Hand Surg Br 1999;24-2:193-8
6. Buijze GA et al. Management of scaphoid nonunion. J Hand Surg Am 2012;37-5:1095-100
7. Szabo RM et al. Displaced fractures of the scaphoid. Clin Orthop Relat Res 1988-230:30-8
8. Ring D et al. Acute fractures of the scaphoid.J Am Acad Orthop Surg 2000;8-4:225-31
9. Herbert TJ, Fisher WE. Management of the fractured scaphoid using a new bone screw. J Bone Joint Surg Br. 1984;66(1):114-123
10. Cooney WP, Dobyns JH, Linscheid RL. Fractures of the scaphoid: a rational approach to management. Clin Orthop Relat Res. 1980(149):90-97
11. Russe O. Fracture of the carpal navicular. Diagnosis, non-operative treatment, and operative treatment. J Bone Joint Surg Am. 1960;42-A:759-768
12. Buijze GA, Ochtman L, Ring D. Management of scaphoid nonunion. J Hand Surg Am. 2012;37(5):1095-100; quiz 1101. doi:10.1016/j.jhsa.2012.03.002.
13. Krimmer H. Management of acute fractures and nonunions of the proximal pole of the scaphoid. J Hand Surg Br. 2002;27(3):245-248. doi:10.1054/jhsb.2001.0736.
14. Adams JE, Steinmann SP. Acute scaphoid fractures. Orthop Clin North Am. 2007;38(2):229-35, vi. doi:10.1016/j.ocl.2007.02.004.
15. Dias JJ. Definition of union after acute fracture and surgery for fracture nonunion of the scaphoid. J Hand Surg Br. 2001, 26: 321-5.

# PART II

## CLASSIFYING SCAPHOID FRACTURES

Rijswijk
A4
Golf Club
Rijswijkse Golfclub
A13
Singel
Rijswijkse Waterweg
Brasserskade
Brasserhout
Wilhelminapark
Tweemolentjesvaart
Het Haantje
Kerstanje
Klein
Delfgauw
Church of Christ
Oude Kerk
Home Goods Store
IKEA Delft
Sion
Delft
Technische
Universiteit
Delft (TU
Delft)
Pr. Beatrixlaan
N473
Zuidwal
Royal Delft
A13
Den Hoorn
Rotterdamseweg
VOORHOF
Bedrijvenpark Ruyver
De Gaag
N470
Buitenhof
A4
Schieweg-Zuid
Tanthof
Golf Course
Stichting
Golfbaan Delfland
Abtswoude
Delftsche
Schie

# Chapter 2

## Classifications of Acute Scaphoid Fractures: A Systematic Literature Review

Journal of Wrist Surgery, 2016
Ten Berg PW, **Drijkoningen T**, Strackee SD, Buijze GA

Abstract

**Background:** In lack of consensus, surgeon-based preference determines how acute scaphoid fractures are classified. There is a great variety of classification systems with considerable controversies.
**Purposes:** The purpose of this study was to provide an overview of the different classification systems, clarifying their subgroups and analyzing their popularity by comparing citation indexes.
The intention was to improve data comparison between studies using heterogeneous fracture descriptions.
**Methods:** We performed a systematic review of the literature based on a search of medical literature from 1950 to 2015, and a manual search using the reference lists in relevant book chapters. Only original descriptions of classifications of acute scaphoid fractures in adults were included. Popularity was based on citation index as reported in the databases of Web of ScienceTM (WoS) and Goolge ScholarTM. Articles that were cited <10 times in WoS, were excluded.
**Results:** Our literature search resulted in 308 potentially eligible descriptive reports of which 12 reports met the inclusion criteria. We distinguished 13 different (sub) classification systems based on 1) fracture location, 2) fracture plane orientation, 3) fracture stability/displacement. Based on citations numbers, the Herbert classification was most popular, followed by the Russe and Mayo classifications. All classification systems were based on plain radiography.
**Conclusions:** Most classification systems were based on fracture location, displacement or stability. Based on the controversy and limited reliability of current classification systems, suggested research areas for an updated classification include three-dimensional fracture pattern etiology and fracture fragment mobility assessed by dynamic imaging.

## INTRODUCTION

Scaphoid fractures were first described in 1905 by Destot followed by the discovery of radiography.[1] These fractures became notorious for their troublesome healing. In 1939, Cravener tried to clarify factors contributing to the establishment of scaphoid nonunion.[2] He encouraged classifying scaphoid fractures taking age and location into account. "In discussing carpal scaphoid fractures, we must first arrive on a common ground. Is the fracture through the tuberosity, the waist, or the body? If it is through the tuberosity we can practically neglect it, for it will hea1. If it is through the body it will not easily." More than seven decades later, it seems that we still haven't arrived on a common ground considering the numerous different scaphoid fracture classification systems available in literature, each trying to improve prognosis and treatment selection. In lack of consensus, surgeon based preference determines how a fracture pattern is classified. Popular classification systems include the Herbert[3], Mayo[4] and Russe[5] classifications, but there are many more and they present considerable controversies. Scaphoid fractures should be characterized in a reliable and reproducible way that facilitates comparisons among different groups or among similar groups treated differently.[6] The use of different classification systems, however, affects comparing outcomes of treatment methods among different clinical trials. An overview of the various classification systems and their subgroups can improve data comparison between studies. The purpose of this study was to review different concepts and classifications of acute scaphoid fractures and their popularity by comparing citation indexes. As incidence rates of different fracture types may vary in literature, our second purpose was to study incidence rates based on the original reports.

## MATERIALS AND METHODS

We conducted a two-step systematic search of medical literature from 1950 to 2015: an online search for original (digital or paper) articles and a manual search for original (digital or paper) articles using a reference lists in relevant book chapters. The online systematic review and data extraction were performed by two independent reviewers (P.W.B; T.D). Disagreements were resolved by means of discussion, with arbitration of a third experienced reviewer (G.A.B.) when differences of opinion remained.

Eligibility criteria systematic review Inclusion criteria for the selection of manuscripts were: (1) original description of a novel classification of the acute scaphoid fracture in an adult population (18 years and older); (2) availability of a (translated) full-text copy of a manuscript online or paper version. We included all types of articles including clinical, biomechanical, cadaveric, imaging studies etc. Exclusion criteria were: (1) (original) description of an already existing classification of acute scaphoid fractures; (2) (original)

description of wrist pathologies other than acute scaphoid fractures; (3) languages other than English, French, or German. Literature search and study selection. The search for articles was performed in Medline (PubMed) in September 2014, and an updated search in October 2015. The search strategy was developed with our academic medical librarian. We used Medical Subject Headings (MeSH) (= scaphoid bone) and MeSH Subheadings (=classification), using free search terms in title and abstract with truncation (=scaphoid fracture*; scaphoid bone fracture*; scaphoid), and using free search terms in all fields with truncation (= class*). This resulted in the following search in Medline: ("Scaphoid Bone"[Mesh] OR scaphoid fracture*[tiab] OR scaphoid bone fracture*[tiab] OR scaphoid[tiab]) AND ("classification" [Subheading] OR class*). We retrieved all titles and abstracts and assessed them for eligibility. If the eligibility criteria were met, full manuscripts were obtained and reviewed. We performed the online search from oldest to most recent article, to identify classifications that were already described.
In addition to online databases, international comprehensive medical books[7-18] regarding the hand, wrist, or scaphoid were available in our academic medical library and included book chapters concerning acute scaphoid fractures. One author (P.W.B) performed a manual search using these book chapters to find additional references. References were further screened in Medline using the same inclusion and exclusion criteria

### Quality assessment

Many different clinical, biomechanical or radiological systems to describe and classify the different acute scaphoid fractures; each with its own characteristics and limitations. To our knowledge, no guidelines have yet been developed to assess the quality of these articles classifying acute scaphoid fractures. Therefore, we didn't make a distinction between study design or image modalities used. Citation numbers Classification systems were considered only clinically relevant when applicable to clinical practice. We used a threshold of >10 times cited in the database of Web of ScienceTM (WoS) for further inclusion in our systematic review. We used Goolge ScholarTM as an additional database to record the number of citations as second measure for popularity of the classifications.

## RESULTS

The online search resulted in 308 potentially eligible articles. Eight met our inclusion criteria. Our manual search resulted in four additional relevant articles (Fig. 1). We pooled two articles describing the original Herbert classification[3] and a modified Herbert classification.[19] In contrast, Böhler[20] and Cooney[4] each discussed two different classification systems. In total, 13 different classification systems were divided based on 1) fracture location, 2) fracture plane orientation, and 3) fracture stability/displacement.

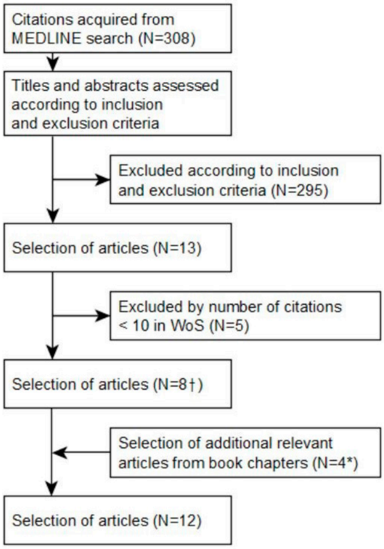


**Figure 1.** Study flow diagram of the systematic review. †Included eight references ; *included four references.

### 1) *Classifications based on fracture location (Table 1).*

Böhler[20] described 873 conservatively treated fractures between 1925 and 1952. Tuberosity fractures showed 100% healing rate; all other fractures 97% rate. Proximal fractures were immobilized for 10-12 weeks, and middle and distal fractures for 6-8 weeks. Cooney[4] (Mayo) (Fig. 2) and Schernberg[21] (Fig. 3) also distinguished fractures by fracture location. Prosser[22] classified solely distal fractures (Fig. 4). Osteoarthritis might develop in the scapho-trapezial-trapezoidal joint due to malunion after compression fractures (type II). The AO foundation introduced a general fracture classification system.[23] To standardize research and communication among surgeons, the Orthopaedic Trauma Association (OTA) adopted this latter system, resulting in the AO/OTA system (Fig. 5).[6]

### 2) *Classifications based on fracture plane orientation (Table 2).*

Böhler[20] also distinguished fractures based on fracture planes, resembling Pauwels classification[24] of femoral neck fractures. Horizontal oblique fractures might show compressive forces across the fracture site resulting in good tendency to heal. Transverse fractures might have both compressive and shear forces resulting in an average tendency to heal. Vertical oblique fractures were considered to be caused by shearing forces, making it unstable with higher risk of nonunion. Russe[5] described a similar system (Fig. 6), which received more attention, probably due to his international publications and presentations. Compson[25] distinguished 80 fractures based on dorsal alignment of fracture planes. He reconstructed the fracture outline on transparent solid 3D scaphoid models by looking at multiple standard radiological views. He separated transverse fractures through the 'surgical waist', oblique fractures through the dorsal sulcus, and proximal pole fractures.

Table 1: Classification of acute scaphoid fractures based on fracture location

| Author | Year | Cited (#)+ | Total cases (#) | Type | | Rate (%) |
|---|---|---|---|---|---|---|
| **1 Böhler (i)*** | **1954** | **38;67** | **873** | **(1)** | **Tuberosity** | **16** |
| | | | | (2)-a | Proximal Third | 10 |
| | | | | (2)-b | Border, middle/ proximal third | 7 |
| | | | | (2)-c | Middle third | 55 |
| | | | | (2)-d | Middle third: wedge chipped out | 4 |
| | | | | (2)-e | Distal third | 9 |
| **2 Cooney (i)** | **1980** | **110;330** | **45** | **1** | **Tuberosity** | ↑ |
| | | | | 2 | Distal articular surface | 16 |
| | | | | 3 | Distal one-third | ↓ |
| | | | | 4 | Waist, middle one third | 67 |
| | | | | 5 | Proximal pole | 18 |
| **3 Schernberg**** | **1984** | **16;37** | **325** | **i** | **Proximal pole** | **4** |
| | | | | ii,iii,iv | Waist | 82 |
| | | | | v | Distal Pole | 8 |
| | | | | vi-,a,b,c | Distal tubercle | 6 |
| **4 Prosser** | **1988** | **13;29** | **37** | **i** | **Tuberosity** | **54** |
| | | | | ii (A,B,C) | Distal intra-articular | 41,0,5 |
| | | | | iii | Osteochondral facture | 0 |
| **5 AO/OTA** | **2007** | **N/A***** | **x** | **72-A1** | **Proximal pole, non-comminuted** | **x** |
| | | | | 72-A2 | Waist, noncomminuted | x |
| | | | | 72-A3 | Distal pole, non-comminuted | x |
| | | | | 72-B2 | Waist, comminuted | x |

+ Number of citations in (World of Science; Google Scholar); *German article; **French article; ***Not applicable, since the article comprised fracture classification systems of the entire musculoskeletal system.

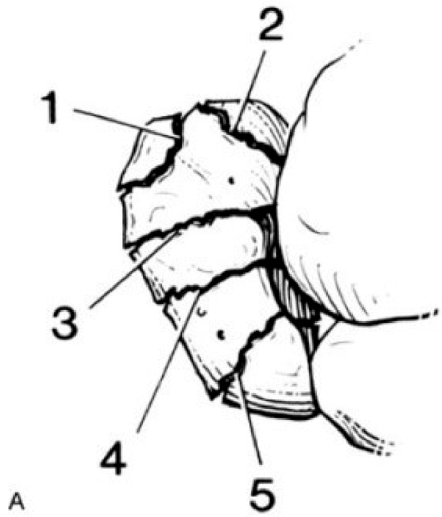


**Figure 2.** Cooney (Mayo) divided scaphoid fractures into fractures of the distal tubercle (1), distal intra-articular surface (2), distal third (3), waist (4), and proximal pole (5). Fracture location influenced both tendency and time frame for healing. (Reprinted, with permission covered by STM guidelines, from Cooney et al.)

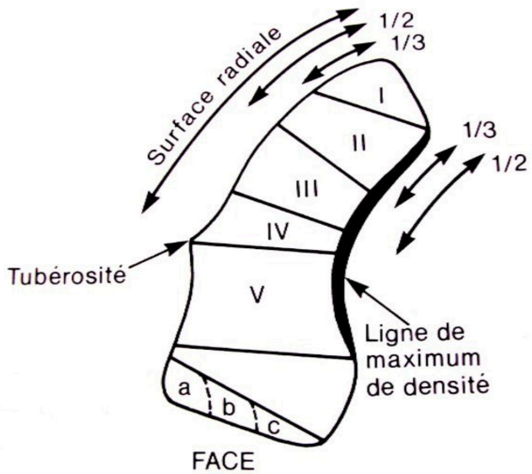


**Figure 3.** Schernberg distinguished six fracture types (I–VI) ranging from the proximal pole to the distal tubercle using the lateral tuberosity and the radial and medial articular surfaces as references. Distal tubercle fractures were further divided into small (a), intermediate (b), or large (c) fragments, and were considered likely to heal successfully, contrary to proximal fractures. (Reprinted, with permission of authors, from Schernberg et al.)

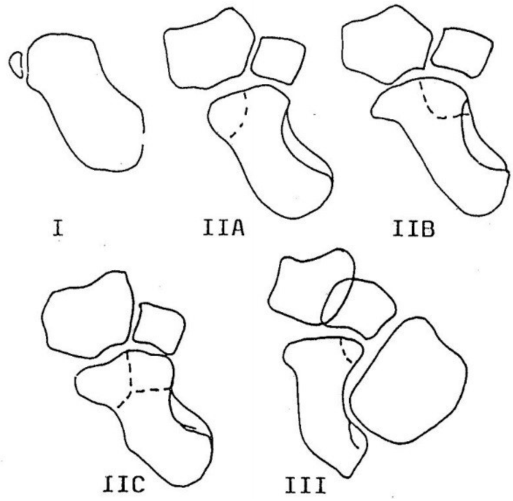


**Figure 4.** Prosser divided distal fractures into avulsion fractures of the tuberosity (I), intra-articular compression fractures of the scaphotrapezial trapezoidal joint including involvement of the radial half (IIA), ulnar half (IIB), or a combination (IIC), and osteochondral fractures at the capitate border (III). All distal fractures were treated by plaster cast. (Reprinted, with permission from Sage publisher, from Prosser et al.)

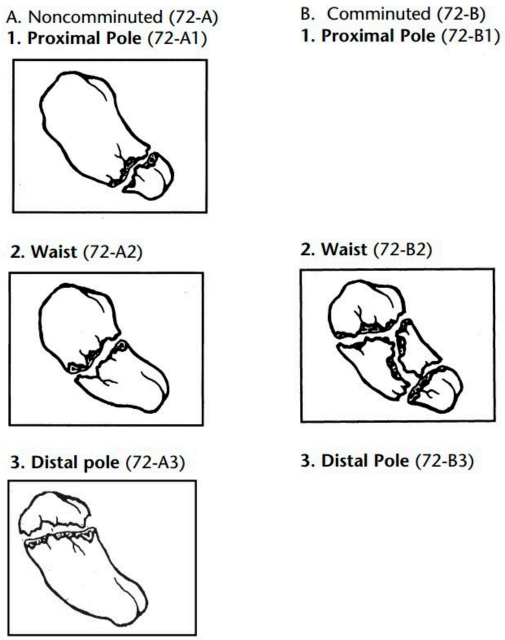


**Figure 5.** In the AO/OTA classification, scaphoid fractures (registered with number 72) were separated into noncomminuted (A) and comminuted (B; more than three fragments) fractures while taking fracture location into account. (Reprinted , with permission covered by STM guidelines, from Marsh et al.)

Table 2: Classification of acute scaphoid fractures based on fracture plane orientation

| Author | Year | Cited (#)+ | Total cases (#) | Type | | Rate (%) |
|---|---|---|---|---|---|---|
| **1 Böhler (i)*** | **1954** | **38;67** | **734** | **HO** | **Horizontal oblique** | **47** |
| | | | | T | Transverse | 50 |
| | | | | VO | Vertical oblique | 3 |
| **2 Russe** | **1960** | **277;501** | **220** | **HO** | **Horizontal oblique** | **35** |
| | | | | T | Transverse | 60 |
| | | | | VO | Vertical oblique | 5 |
| **3 Compson** | **1998** | **41;69** | **80** | **1** | **Transverse waist (Surgical waist)** | **30** |
| | | | | 2 | Oblique waist (Dorsal Sulcus) | 36 |
| | | | | 3 | Proximal pole | 34 |

+ Number of citations in (World of Science; Google Scholar); *German article

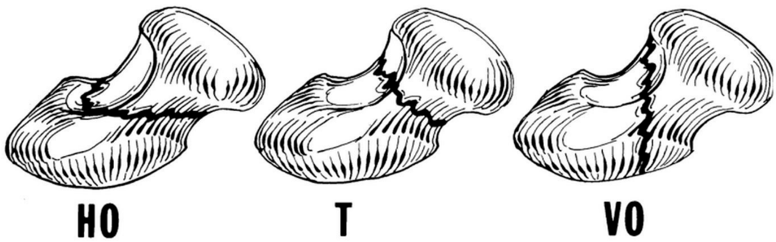


Figure 6. Russe separated fractures based on fracture plane orientation into transverse (T), horizontal oblique (HO), and vertical oblique (VO) fractures. Vertical oblique fractures were most troublesome with healing, requiring longer immobilization time (10–12 weeks). (Reprinted, with permission from Elizabeth Roselius, from Taleisnik.)

Table 3: Classification of acute scaphoid fractures based on displacement/instability

| Author | Year | Cited (#)+ | Total cases (#) | Type | | Rate (%) |
|---|---|---|---|---|---|---|
| **1 McLaughlin** | **1969** | **37;70** | **x** | **A** | **Incomplete** | **x** |
| | | | | B | Undisplaced and stable | x |
| | | | | C | Displaced and unstable | x |
| **2 Cooney (ii)** | **1980** | **110;330** | **45** | **1** | **Nondisplaced/stable** | **71** |
| (Mayo) | | | | 2 | Displaced/unstable | 29 |
| **3 Weber** | **1980** | **35;127** | **36** | **1** | **Nondisplaced** | **53** |
| | | | | 2 | Angulated | 17 |
| | | | | 3 | Displaced | 30 |
| **4 Herbert/** | **1984/** | **331;739** | **200/** | **A1** | **Stable, Tubercle** | **x** |
| Modified | 1996 | 139;268 | 431 | A2 | Stable, incomplete waist | x |
| Herbert | | | | B1 | Unstable, Distal oblique | 19* |
| | | | | B2 | Unstable, Complete waist | 60* |
| | | | | B3 | Unstable, Proximal pole | 21* |
| | | | | B4 | Unstable fracture dislocation | x |
| | | | | B5 | Unstable, Comminuted** | x |
| **5 Garcia-** | **2001** | **27;53** | **x** | **1** | **Stable, proximal to SL-ligament** | **x** |
| **Elias** | | | | 2 | Unstable, distal to SL-ligament | x |

+ Number of times cited based on (World of Science;Google Scholar); *Based on 82 B1, B2 and B3 fractures reported in the article of 1996; **Omitted in the modified Herbert classification

### *3) Classifications based on displacement and/or instability (Table 3).*

McLaughin[26] classified fractures by their stability ranging from incomplete fractures with intact shell of cartilage and bone to undisplaced/stable fractures and displaced/unstable fractures. Cooney[4] (Mayo) also classified fractures by their stability (Table 4). Based on biomechanical experiments, Weber[27] described nondisplaced fractures without disruption of ligamentous attachments, angulated fractures with dorsal intercarpal ligamentous disruption due to increasing injury forces, and displaced fractures with complete disruption of ligamentous attachments. Angulation may decrease the amount of surface contact, thus increasing risk of nonunion. Herbert[3,19] proposed a classification with the intention to identify fractures most applicable for screw fixation, due to instability (Fig. 7). All complete bicortical fractures (except for tubercle fractures) were considered unstable. According to Garcia-Elias[28], proximal scaphoid fractures are stable when running proximal to the scaphoid-lunate ligaments which form the important linkage between the lunate and the distal scaphoid, but are unstable when running distal to them.



**Table 4: Mayo Classification based on instability of acute scaphoid fractures and their characteristics**

| Stable fracture | Unstable fracture |
|---|---|
| Displacement < 1mm | Displacement > 1mm |
| Normal intercarpal alignment | DISI* alignment |
| capitate-lunate angle 0⁰ to 15⁰ | capitate-lunate angle >15⁰ |
| scaphoid-lunate angle 30⁰ to 60⁰ | scaphoid-lunate angle > 60⁰ |
| Lateral intrascaphoid angle < 35⁰ | Lateral intrascaphoid angle >35⁰ |
| Distal fractures | Comminuted fractures |
| | Perilunate fractures |

* DISI: Dorsal intercalated segmental instability

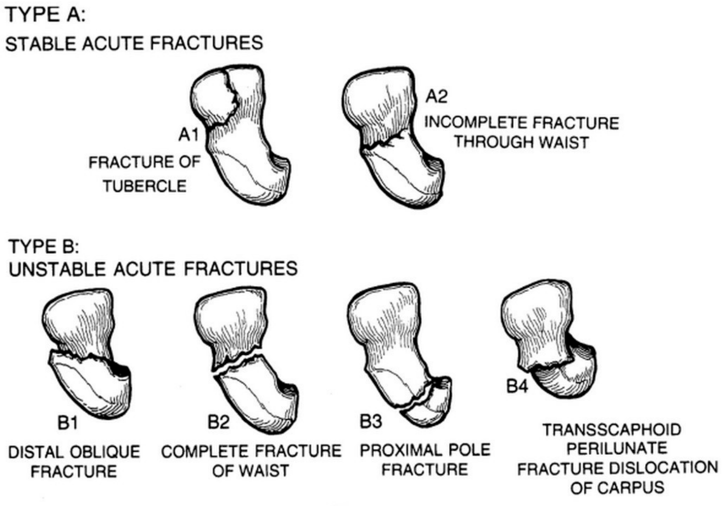


**Figure 7.** Herbert divided acute scaphoid fractures into acute stable (**A**) and unstable (**B**). Stable acute fractures included fractures of the tubercle and incomplete unicortical "crack" fractures. Only this type unites relatively fast and should be treated with a cast. (Reprinted, with permission covered by STM guidelines, from Green DO, ed. Operative Hand Surgery. 3rd ed. New York, NY: Churchill Livingstone; 1993.)

## DISCUSSION

In the past few decades, much endeavor has been done to identify the acute scaphoid fracture patterns that are prone to nonunion for purposes of surgical decision making. Based on our search, over a dozen classification systems have been proposed in literature and were mainly based on fracture location or displacement. Considering the number of citations, the Herbert classification was most popular, followed by the Russe and Mayo classification. Based on original reports describing fracture location,[4,20,21] waist fractures occur most often with percentages ranging from 66 to 82%. Considering fracture plane orientation,[5,20,25] transverse fractures have the highest incidence ranging from 36% to 60%, followed by horizontal oblique fractures ranging from 30% to 47%. Considering fracture stability,[4,27] most fractures are described as stable (53% and 71%). Based on two recent systematic reviews,[29,30] several randomized controlled trials can be identified comparing surgical with conservative treatment for acute scaphoid fractures using various radiographic classification systems including those described by Herbert,[31-34] the AO/OTA[35] and Russe. [34] Inclusion criteria ranged from waist fractures only[31-33,36] to distal, waist and proximal fractures[34,35,37], or from only nondisplaced[31,32,36] to minimally, moderately and severely displaced fractures.[33,34,37] Some trials[32,34,35,37] excluded tuberosity and unicortical fractures. One trial[35] included vertical and comminuted fractures. In most trials, the exact borders of the waist area and level of displacement/step-off were not defined. In particular, it is often unclear when displacement is considered to be minimal. Based on interobserver studies, agreement regarding the radiographical assessment of fracture displacement varies between fair,[38] moderate[39] and good.[40] Displacement close to 1 mm can be easily misclassified as nondisplacement.[41] Encouraging results have shown that training can improve interobserver reliability and diagnostic performance for fracture displacement.[42] In another interobserver study,[39] agreement between observers was only fair regarding the radiographical classification of scaphoid fractures according to Compson, Herbert and Russe. Observers had difficulty with each classification system and neither did significantly better than the other. None of the systems could predict fracture union. In general, fracture lines as observed on radiographs are difficult to relate to the three-dimensional complex anatomy[25] and sometimes difficult to detect due to superimposition over neighboring carpal bones.[43] Recently, Luria et al.[44] used three-dimensional imaging techniques to analyze fracture plane orientation relative to the scaphoid central axis in acute scaphoid fractures. They concluded all fractures were horizontal oblique, and not transverse, unlike previous radiographically observational studies have reported. It seems that the variation of used radiographic classification systems and their limited reliability confound efforts to compare outcomes of treatment methods among different clinical studies, limiting the level of evidence.[45] When distinguishing fractures, the clinical relevance must be clear in relation to either treatment options, prognosis or risk of complications. At the waist of the scaphoid, displaced fractures are considered unstable, which is the most important factor associated with nonunion, for which open reduction and internal fixation is generally advised.[46,47] However, when displacement is not clearly visible on radiographs, as in most patients, potentially unstable scaphoid fractures are difficult to identify. Some surgeons consider all fractures unstable, irrespective to displacement, when the fracture line is readily identified on radiographs[48] or show bicortical involvement[49] and suggest operative treatment. Firstly, this may lead to overtreatment as the incidence of unstable fractures being classified as nondisplaced is currently unknown as well as their relative risk of nonunion. Secondly, in a previous study[50] using arthroscopy as reference standard for instability and displacement, only 7 of 22 radiographically nondisplaced (bicortical) fractures were unstable. We believe that after confirming a scaphoid fracture, management could be further improved if we find a more reliable way to identify substantial interfragmentary motion when displacement is ruled out. Imaging modalities with the wrist in motion using fluoroscopy and dynamic three-dimensional CT may be useful to find predictors for interfragmentary motion (i.e. true instability) in relation to surgical or arthroscopic findings and clinical outcome. To date, one possible predictor of acute fracture instability might be the location relative to the dorsal apex as shown in nonunions.[51] However, this factor was not predictive for instability in one previous study[52] of acute fractures using arthroscopy as a reference standard. Fracture comminution was the only significant predictor for instability. Considering the fact that the majority of nondisplaced fractures are treated conservatively, predicting instability might improve identification of the small subset of scaphoid fractures unlikely to heal in a cast.

## REFERENCES


1. Peltier LF. The classic. Injuries of the wrist. A radiological study. By Etienne Destot.1926. Clin Orthop Relat Res. 1986(202):3-11
2. Cravener EK, McElroy DG. Fractures of the Carpal (Navicular) Scaphoid. American Journal of Surgery. 1939;44(1):8
3. Herbert TJ, Fisher WE. Management of the fractured scaphoid using a new bone screw. J Bone Joint Surg Br. 1984;66(1):114-123
4. Cooney WP, Dobyns JH, Linscheid RL. Fractures of the scaphoid: a rational approach to management. Clin Orthop Relat Res. 1980(149):90-97
5. Russe O. Fracture of the carpal navicular. Diagnosis, non-operative treatment, and operative treatment. J Bone Joint Surg Am. 1960;42-A:759-768
6. Marsh JL, Slongo TF, Agel J, et al. Fracture and dislocation classification compendium - 222 2007: Orthopaedic Trauma Association classification, database and outcomes committee. J Orthop Trauma. 2007;21(10 Suppl):S1-133
7. Green DP, ed Operative Hand Surgery. 2nd ed. New York: Churchill Livingstone; 1988; No. 2
8. Tubiana R, ed The Hand. 1st ed. Philadelphia: W.B, Saunders Company 1985; No. 2
9. Tubiana R, Slade III JF, eds. Hand Clinics: Scaphoid Fractures. 1st ed. Philadelphia: W.B. Saunders Company; 2001; No. 17
10. Nakamura R, Linscheid RL, Miura T, eds. Wrist Disorders. 1st ed. Tokyo: Springer- Verslag; 1992; No. 1st
11. Sandzen SC. Atlas of Wrist and Hand Fractures 2nd ed. Littleton: PSG Publishing Company; 1986
12. Barton NJ, ed Hand and Upper 233 Limb: Fractures of the Hand and Wrist. 1st ed. New York: Churchill Livingstone; 1988; No. 4
13. Cooney WP, Linscheid RL, Dobyns JH, eds. The Wrist Diagnosis and Operative Treatment. 1st ed. St. Louis: Mosby; 1998; No. 1
14. Lichtman DM, Herbert Alexander A, eds. The Wrist and its Disorders Second ed. Philadelphia: W.B. Saunders 1997
15. Taleisnik J. The wrist. 1st ed. New York: Churchill Livingstone 1985
16. Razemon JP, Fisk GR, eds. The Wrist. 1st ed. New York: Churchill Livingstone; 1988
17. Sennwald G. The Wrist. 1st ed. Berlin: Springer-Verlag; 1987
18. Slutsky DJ, Slade JF, eds. The Scaphoid. 1st ed. New York: Thieme Medical; 2010
19. Filan SL, Herbert TJ. Herbert screw fixation of scaphoid fractures. J Bone Joint Surg Br.1996;78(4):519-529
20. Bohler L, Trojan E, Jahna H. [Treatment of 734 cases of fresh fracture of the scaphoid bone of the hand]. Wiederherstellungschir Traumatol. 1954;II:86-111
21. Schernberg F, Elzein F, Gerard Y. [Anatomo-radiological study of fractures of the carpal scaphoid bone. Problems of abnormal callus]. Rev Chir Orthop Reparatrice Appar Mot. 984;70 Suppl 2:55-63
22. Prosser AJ, Brenkel IJ, Irvine GB. Articular fractures of the distal scaphoid. J Hand Surg Br. 1988;13(1):87-91

23. Müller ME, Allgöwer M, Willenegger H. Technik der operative Frakturenbehandlung. 1st ed. Berlin: Springer; 1963
24. Pauwels F. Der schenkelhalsbruch ein mechanisches problem: Grundlagen des Haeilungsvorganges Prognose und kausale Therapie. . Stuttgart: Ferdinand Enke Verlag; 1935.
25. Compson JP. The anatomy 257 of acute scaphoid fractures: a three-dimensional analysis of patterns. J Bone Joint Surg Br. 1998;80(2):218-224
26. McLaughlin HL, Parkes JC, 2nd. Fracture of the carpal navicular (scaphoid) bone: gradations in therapy based upon pathology. J Trauma. 1969;9(4):311-319
27. Weber ER. Biomechanical implications of scaphoid waist fractures. Clin Orthop Relat Res. 1980(149):83-89
28. Garcia-Elias M, Lluch A. Partial excision of scaphoid: is it ever indicated? Hand Clin. 2001;17(4):687-695, x
29. Buijze GA, Doornberg JN, Ham JS, Ring D, Bhandari M, Poolman RW. Surgical compared with conservative treatment for acute nondisplaced or minimally displaced scaphoid fractures: a systematic review and meta-analysis of randomized controlled trials. J Bone Joint Surg Am. 2010;92(6):1534-1544
30. Symes TH, Stothard J. A systematic review of the treatment of acute fractures of the scaphoid. J Hand Surg Eur Vol. 2011;36(9):802-810
31. Adolfsson L, Lindau T, Arner M. Acutrak screw fixation versus cast immobilisation for undisplaced scaphoid waist fractures. J Hand Surg Br. 2001;26(3):192-195
32. Arora R, Gschwentner M, Krappinger D, Lutz M, Blauth M, Gabl M. Fixation of nondisplaced scaphoid fractures: making treatment cost effective. Prospective controlled trial. Arch Orthop Trauma Surg. 2007;127(1):39-46
33. McQueen MM, Gelbke MK, Wakefield A, Will EM, Gaebler C. Percutaneous screw fixation versus conservative treatment for fractures of the waist of the scaphoid: a prospective randomised study. J Bone Joint Surg Br. 2008;90(1):66-71
34. Vinnars B, Pietreanu M, 279 Bodestedt A, Ekenstam F, Gerdin B. Nonoperative compared with operative treatment of acute scaphoid fractures. A randomized clinical trial. J Bone Joint Surg Am. 2008;90(6):1176-1185
35. Saeden B, Tornkvist H, Ponzer S, Hoglund M. Fracture of the carpal scaphoid. A prospective, randomised 12-year follow-up comparing operative and conservative treatment. J Bone Joint Surg Br. 2001;83(2):230-234
36. Bond CD, Shin AY, McBride MT, Dao KD. Percutaneous screw fixation or cast immobilization for nondisplaced scaphoid fractures. J Bone Joint Surg Am. 2001;83- A(4):483-488
37. Dias JJ, Wildin CJ, Bhowal B, Thompson JR. Should acute scaphoid fractures be fixed? A randomized controlled trial. J Bone Joint Surg Am. 2005;87(10):2160-2168
38. Lozano-Calderon S, Blazar P, Zurakowski D, Lee SG, Ring D. Diagnosis of scaphoid fracture displacement with radiography and computed tomography. J Bone Joint Surg Am. 2006;88(12):2695-2703
39. Desai VV, Davis TR, Barton NJ. The prognostic value and reproducibility of the radiological features of the fractured scaphoid. J Hand Surg Br. 1999;24(5):586-590

40. Bhat M, McCarthy M, Davis TR, Oni JA, Dawson S. MRI and plain radiography in the assessment of displaced fractures of the waist of the carpal scaphoid. J Bone Joint Surg Br. 2004;86(5):705-713
41. Temple CL, Ross DC, Bennett JD, Garvin GJ, King GJ, Faber KJ. Comparison of sagittal computed tomography and plain film radiography in a scaphoid fracture model. J Hand Surg Am. 2005;30(3):534-542
42. Buijze GA, Guitton TG, van Dijk CN, Ring D, Science of Variation G. Training improves interobserver reliability for the diagnosis of scaphoid fracture displacement. Clin Orthop Relat Res. 2012;470(7):2029-2034
43. Moritomo H. Radiographic clues for determining carpal instability and treatment protocol for scaphoid fractures. J Orthop Sci. 2014;19(3):379-383
44. Luria S, Schwarcz Y, Wollstein R, Emelife P, Zinger G, Peleg E. 3-dimensional analysis of scaphoid fracture angle morphology. J Hand Surg Am. 2015;40(3):508-514
45. Bruinsma WE, Guitton TG, Warner JJ, Ring D, Science of Variation G. Interobserver reliability of classification and characterization of proximal humeral fractures: a comparison of two and three-dimensional CT. J Bone Joint Surg Am. 2013;95(17):1600-1604
46. Buijze GA, Ochtman L, Ring D. Management of scaphoid nonunion. J Hand Surg Am. 2012;37(5):1095-1100; quiz 1101
47. Swart E, Strauch RJ. Diagnosis of scaphoid fracture displacement. J Hand Surg Am. 2013;38(4):784-787; quiz 787
48. Steinmann SP, Adams JE. Scaphoid fractures and nonunions: diagnosis and treatment. J Orthop Sci. 2006;11(4):424-431
49. Herbert TJ. The Fractured Scaphoid 1st ed. St. Louis: Quality Medical Publishing; 1990
50. Buijze GA, Jorgsholm P, Thomsen NO, Bjorkman A, Besjakov J, Ring D. Diagnostic performance of radiographs and computed tomography for displacement and instability of acute scaphoid waist fractures. J Bone Joint Surg Am. 2012;94(21):1967-1974
51. Moritomo H, Murase T, Oka K, Tanaka H, Yoshikawa H, Sugamoto K. Relationship between the fracture location and the kinematic pattern in scaphoid nonunion. J Hand Surg Am. 2008;33(9):1459-1468
52. Buijze 325 GA, Jorgsholm P, Thomsen NO, Bjorkman A, Besjakov J, Ring D. Factors associated with arthroscopically determined scaphoid fracture displacement and instability. J Hand Surg Am. 2012;37(7):1405-1410


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Schilderswijk
Oude Haagweg
LAAK
De la Reyweg
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Burgemeester Elsenlaan
Moerwijk
Morgenstond
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# Chapter 3

## Scaphoid Fracture Patterns. Part One: Three-dimensional Computed Tomography Analysis

Journal of Wrist Surgery
**Drijkoningen T**, Mohamadi A, Luria S, Buijze GA

**Purpose**: Using three-dimensional (3D) computed tomography models of acute scaphoid fractures we looked for differences between volumetric size of the fracture fragments of fracture fragments, recognizable groups, or a shared common fracture area.
**Methods**: We studied 51 patients with an adequate computed tomography scan of an acute scaphoid fracture using 3D modeling. Fracture surfaces were identified and fragment volumetric size of the fracture fragments was measured. Principal component analysis was used trying to find groups of similar fracture patterns. Density mapping was used to image probable common fracture areas in the scaphoid.
**Results**: Forty-nine of 51 fractures had a similar pattern. It was not possible to identify subgroups based on fracture pattern. The mean volumetric size of the fracture fragments of the proximal (1.45 cm3 +/- 0.49 cm3 SD) and distal fracture fragments (1.53 cm3 +/- 0.48 cm3 SD) was similar. There was a single common fracture area in the middle third of the bone. In the distal third there were no horizontal fractures through -- but only directly proximal to-- the tubercle suggesting that these would be best classified as distal waist fractures.
**Conclusion**: Acute scaphoid fractures mainly occur in the middle third of the bone, and tend to divide the scaphoid in half by volumetric size of the fracture fragments. There were two distinct grouping patterns: fractures through the proximal and middle third were horizontal oblique whereas fractures of the distal third were vertical oblique. It seems that scaphoid fractures might be classified into proximal pole fractures, a range of waist fractures and tubercle avulsion fractures.
**Level of evidence:** Level IV

# INTRODUCTION

If we can identify specific scaphoid fracture patterns, we might use different fixation strategies. For instance, a screw along the longitudinal axis of the scaphoid may be optimal if the fracture is 90 degrees to this axis, but fractures angled 50 to 55 degrees with respect to the longitudinal axis may be stabilized better by a slightly off axis screw.

To better understand scaphoid fracture appearance on radiographs, Compson evaluated 50 healthy scaphoid cadaver bones.[1] He then selected 10 bones that he felt represented important variations in pattern and anatomical features and made 10 clear methylmethacrylate models. Using radiographs of 91 scaphoid fractures, he then selected a scaphoid model of appropriate pattern and size selected from the set of 10 models over radiographs and drew the fracture lines on the model. He found that 80 of the fractures could be captured in 3 different classes: the 'surgical waist'; the dorsal sulcus; and the proximal pole.

Currently we can create three-dimensional models of the scaphoid directly from CT-scans using a computer. Luria *et al* used 124 scaphoid models to study scaphoid fracture angle morphology using a precise computerized 3-dimensional technique. They classified 86 as waist fractures, 13 distal third, and 25 proximal third. Most fractures had a volar distal to dorsal proximal horizontal oblique inclination relative to the volar dorsal vector with a mean angle of 53 degrees for waist fractures.[2]

The purpose of this study was to distinguish the various groups of acute scaphoid fracture patterns using 3D models. The primary hypothesis was that the relative volumetric size of the fracture fragments would divide the scaphoid into two comparable fragments and that a shared common fracture area can be defined.

# MATERIAL AND METHODS

## Selection of CT-scans

After our institutional review board approved the study, we performed a retrospective search of billing data to identify patients with a scaphoid fracture between January 2003 and December 2014 at 2 level I trauma centers. Using the International Classification of Diseases, Ninth Revision, Clinical Modification codes (814.01 for closed fracture and 814.11 for open fracture); we identified 1064 patients with scaphoid fractures. Inclusion criteria were patients aged 18 years or older with a fracture of the scaphoid; a computed tomography (CT) scan performed within 30 days of injury; CT scan available and slice thickness 1.25 mm or less and displaying the complete scaphoid bone.

A total of 51 patients (4 with proximal pole and 47 with scaphoid waist fractures) met the inclusion criteria. Our study sample consisted of 41 men and 10 women with a mean age of 33 years (SD=13). Twenty-five (51%) of the scaphoid fractures involved the right hand. Thirty-five of the fractures were non-displaced, 16 were displaced. None of the fractures were comminuted. All displaced fractures were reduced to fit the template bone. The template bone was a 3D reconstructed non fractures healthy scaphoid using a CT-scan of a patient suspected of a fracture. Also 35 (69%) patients had an isolated scaphoid fracture, in 16 (31%) of the cases another bone in the wrist or hand was also fractured. Surgery was performed in 28 (55%) of the cases. Of all patients, 2 (4%) had a nonunion after conservative treatment.

## Modeling of Scaphoid Bone

We obtained the original Digital Imaging and Communications in Medicine (DICOM) files of selected CT scans through the Picture Archiving Communications System database of the 2 hospitals. The DICOM CT-scans were loaded into 3D Slicer (Boston, MA), a software program used for analysis and visualization of medical images. CT-scans are shown in the program in 3 different manners namely transverse, sagittal, and oblique. The scaphoid was manually marked per CT-slice on transverse, sagittal, and oblique CT slides to get closest to the true fracture. Paint Effect was used to mark the scaphoid in 2 different colours and the Threshold Paint option was used to make sure only the scaphoid was marked. Voxels within the predefined threshold range (250-1760 Hounsfield units) were labeled and annotated as bone. After marking the scaphoid, the two fracture fragments separately on each CT cut, we created 3-dimensional polygon mesh reconstructions consisting of 2 fracture parts in different colors.

## Fracture Surface

The 3-dimensional mesh reconstructions were imported into Rhinoceros (McNeel, Seattle, WA) for further analyses. The volumetric size of the fracture fragments of scaphoid fracture fragments was measured using the standard volume command in Rhinoceros. Subsequently, a template scaphoid bone was used to fit all 51 scaphoid fracture cases. The template bone was enclosed in a rectangular shaped box to standardize the position in space of every fracture. The articular surface area was marked with a polyline on the mesh reconstructions and measured using the area command after splitting the mesh surface with the applied polyline. After creating the fracture surfaces, the x, y, z coordinates were extracted per fracture plane and exported to excel. The mesh reconstructions in the scaphoid template were also visualized using density mapping. For the density mapping all 3D reconstructed scaphoid bones were projected on each other. (Figure 1) The darker the color in the density map, the more fracture planes overlapped in that specific voxel. So a lighter color means that less voxels of fracture planes overlapped in those voxels. Fractures location was defined geometrically according to the third of bone that involved the full or largest part of the fracture (e.g. if 70% of the fracture line involved the middle third and 30% the distal third, it would be classified as a middle third fracture).

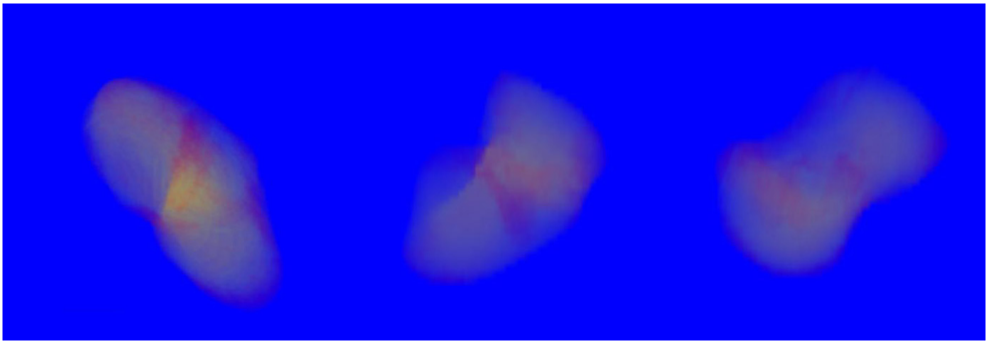

**Figure 1.** Density map of 51 scaphoid fractures



## Statistical analyses

Baseline characteristics of study patients were summarized with frequencies and percentages for categorical variables and with means and standard deviations for continuous variables. To calculate the proximity of the different fractures, we projected, for each subject, the fracture points onto the plane of the first two principal components, and also onto the vector orthogonal to this surface. The first projection provided an estimate of the fracture plane, and the second projection measured deviation from this plane. We centered the projected points for each subject, determined the smallest convex region containing these points (i.e., the convex hull), and also the boundary and area of this circumscribed region. We used the projection on the out-of-plane vector to check for non-planar fractures, and a plot of the superposition of the convex hull perimeters, centered at a common origin, to check for unusual fracture patterns. After removing outliers, we used hierarchical agglomerative clustering to attempt to cluster the fracture patterns.

# RESULTS

Of the 51 fractures, 6 seemed to be proximal and 45 waist fractures. In our cohort no distal fractures were found. Forty-nine of 51 fractures had a similar pattern (Figure 2). It was not possible to identify subgroups based on fracture pattern. The mean volumetric size of the fracture fragments of the proximal fracture fragments was 1.45 $cm^3$ (0.49 $cm^3$ SD) and the mean volumetric size of the fracture fragments of the distal fragments was 1.53 $cm^3$ (0.48 $cm^3$ SD). Density maps also identified one similar horizontal oblique pattern of fractures, although we found an area in the middle of the scaphoid bone where most fractures were situated. We found 6 proximal pole fractures. Although several fractures were located directly proximal to distal tubercle, none of these fractures was (predominantly) located in the distal third, of the scaphoid bone. Fractures were defined as distal if they were originated in the STT joint.

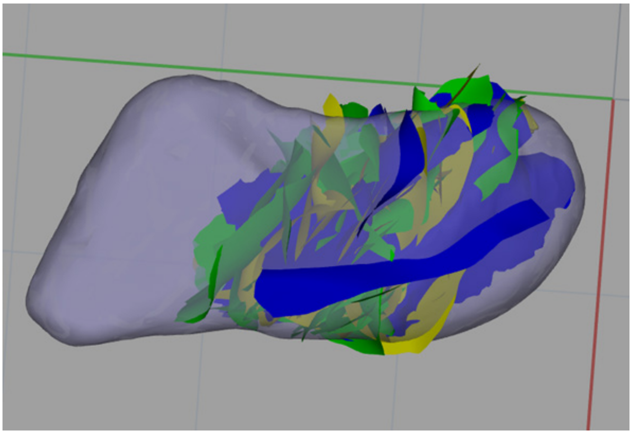

**Figure 2.** 51 Patients fracture maps in Rhinoceros

## DISCUSSION

This study showed that all scaphoid fractures in the proximal and middle third of the bone were similar horizontal oblique type fractures with a single common fracture area in the middle third of the bone. None of the most distal fractures went through -- but only directly proximal to-- the tubercle suggesting that these would be best classified as distal waist fractures. To investigate whether these notable findings were consistent with larger series a secondary analysis of a similar previously published series of 124 scaphoid models was performed including 13 distal third fractures.[2] In this series using comparable imaging techniques and definitions, the distinct fracture patterns were identical –12 distal third fractures were oriented vertical oblique through the scaphoid tubercle, involving the scapho-trapezio-trapezoid (STT) joint. (Figure 3) This type of distal third fracture is more commonly referred to as a scaphoid tubercle fracture.[3]

Scaphoid fractures are classified largely by location, but also by displacement, fracture orientation, and healing stage.[4] It is not clear that there are distal third, non tubercle fractures that are distinct from waist fractures. Consistent with the series of Luria *et al,* we found that the vast majority of distal (pole) scaphoid fractures can be classified in two types according to whether or not they involve the tubercle: distal waist fractures (horizontal oblique directly proximal to the tubercle) and tubercle fractures (vertical avulsion type fractures through the tubercle). It is also difficult to draw a clear line between fracture of the proximal scaphoid and fractures of the scaphoid waist as there is no distinct pattern between these types of fractures. Using 3D-CT and fracture mapping, the vast majority of fractures were in the middle third of the bone and split the scaphoid in half by volumetric size of the fracture fragments.

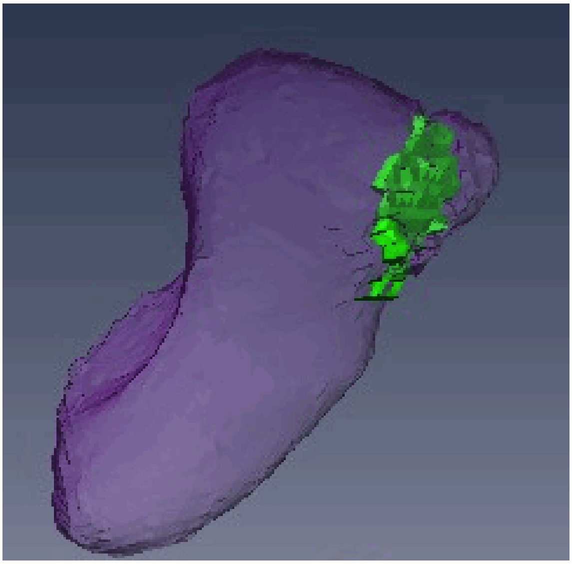

**Figure 3.** Scaphoid fracture map for tubercle fracture



Study limitations include the highly selective group of patients with a CT-scan with a slice thickness 1.25 mm or smaller. This introduces sampling bias as the subset of patients may not be representative of the average patient with a scaphoid fracture. In particular, these fractures were likely either difficult to diagnose on radiographs or they were evaluated for the likelihood of displacement. Our impression is that these fractures are most representative of the subset of fractures that are more than a small distal tubercle fracture. The second limitation is that a healthy scaphoid was used as a template for mapping fractured scaphoids. There is significant variation in the size of the scaphoid although this doesn't change the location of the fracture. This may have introduced a small amount of error and variation based on size of the scaphoid and alignment of the fracture.

If the scaphoid is smaller, and there is a fracture through the waist, the size of the fractured scaphoid doesn't change its location.

In general, acute scaphoid fractures divide the scaphoid roughly in half by volumetric size of the fracture fragments. This is an interesting finding that to our knowledge has not been previously reported. It seems that there is less variation in fracture morphology and fracture size than previously imagined. As Compson noted, the variability on radiographs exaggerates the actual variability.[1] There seems to be a general mid-waist fracture area that divides the scaphoid roughly in half.

Although we didn't find a statistical significant pattern, our density map shows the suggestion of a common fracture area in the middle third of the bone. This supports our thought that there is a continuous range of fractures in the middle third of the scaphoid bone rather than discrete categories (with exception of the tubercle fractures).

Some of these might appear to involve the distal third depending on the position of the wrist and the projection of the radiographs. Patients with distal tubercle fractures uncommonly get CT scans, so none were included in this series. The current study shows that the vast majority of fractures can be classified on posteroanterior imaging of the scaphoid as (1) proximal pole fractures (proximal to the distal scapholunate (SL) interval), (2) a range of waist fractures (involving the scaphocapitate (SC) interval), and (3) distal tubercle fractures (involving the STT interval). Using this simplified anatomical classification system, the fracture is classified on posteroanterior radiographs based on the involvement of the adjacent joint interval as proximal (SL), waist (SC) or distal (STT) (Figure 4). Rarely have scaphoid fractures been reported that do not fit this classification, such as coronal plane fractures and distal horizontal oblique fractures that seem to involve both the tubercle and the scaphocapitate interval.[5,6]

Many physicians have tried to classify and understand scaphoid fractures and their outcome using various techniques. Using fracture pattern, fracture fragment volumetric size of the fracture fragments and density mapping in a 3D setting we found a fracture area in the middle third of the bone but couldn't classify those fractures using the principal component analysis as all fractures through the proximal and middle third were horizontal oblique. There was only one distinct group of fractures of the distal third, which were vertical oblique described by Luria *et al.* It seems that scaphoid fractures might be classified into proximal pole fractures, a range of waist fractures and tubercle avulsion fractures. A future study might compare plain film "assessment" of scaphoid fractures with CT scan volumetric fracture fragments as often surgeons judge scaphoid fracture patterns and fracture repair on radiographs alone.

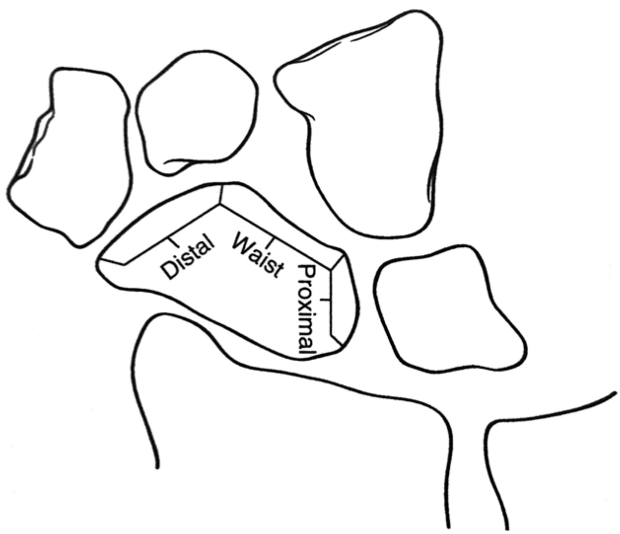


**Figure 4.** Simplified classification; distal, waist and proximal pole fractures

## REFERENCES

1. Compson JP. The anatomy of acute scaphoid fractures: a three-dimensional analysis of patterns. J Bone Joint Surg Br. 1998;80:218-224.
2. Luria S, Schwarcz Y, Wollstein R, Emelife P, Zinger G, Peleg E. 3-dimensional analysis of scaphoid fracture angle morphology. J Hand Surg Am. 2015 Mar;40(3):508-514. doi: 10.1016/j.jhsa.2014.11.008. Epub 2015 Jan 9
3. Kraus R, Böhringer G, Meyer C, Stahl JP, Schnettler R. [Fractures of the scaphoid tubercle]. Handchir Mikrochir Plast Chir. 2005 Apr;37(2):79-84. German.
4. Ten Berg PW, Drijkoningen T, Strackee SD, Buijze GA. Classifications of Acute Scaphoid Fractures: A Systematic Literature Review. J Wrist Surg. 2016 May;5(2):152-159. doi: 10.1055/s-0036-1571280. Epub 2016 Jan 15.
5. Oron A, Gupta A, Thirkannad S. Nonunion of the scaphoid distal pole. Hand Surg. 2013;18(1):35-39. doi: 10.1142/S0218810413500068.
6. Slutsky DJ, Herzberg G, Shin AY, Buijze GA, Ring DC, Mudgal CS, Leung YF, Dumontier C. Coronal Fractures of the Scaphoid: A Review. J Wrist Surg. 2016 Aug;5(3):194-201. doi: 10.1055/s-0036-1585414. Epub 2016 Jul 11.

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Noorderkwartier
Langegracht
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Hooglandse Kerk
De Waard
Hoge Rijndijk
Levendaal
Sports Complex
Sportpark Boshuizerkade
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# Chapter 4

## Scaphoid Fracture Patterns Part Two; Demographics associated with acute tubercle, waist and proximal pole fractures of the scaphoid

Journal of Wrist Surgery
**Drijkoningen T**, Mohamadi A, van Leeuwen WF, Schwarz Y, Ring DC, Buijze GA

**Purpose:** To analyze the reproducibility, reliability and demographics of a simplified anatomical scaphoid fracture classification based on posteroanterior radiographs using a large database of scaphoid fractures.
**Methods:** The study consisted of a retrospective review of electronic medical records of 871 consecutive patients. All patient presented between 2003 and 2014 at two centers. Patient and surgeon related factors were analyzed. Additionally, inter-observer reliability of the Herbert and simplified scaphoid fracture classifications were tested.
**Results:** Proximal pole were defined as fractures in which the center of the fracture line was proximal to the distal scapholunate interval (n=30), waist fractures (n=802) were defined as fractures involving the scaphocapitate interval and distal tubercle fractures (n=39) were defined as fractures involving the scapho-trapezio-trapezoid interval. The inter-observer reliability of the simplified classification was fair ($\kappa$ =0.37) as for the Herbert classification ($\kappa$ =0.31). The average doubt of the answers of the observers was 2.1 on a scale from 0-10 for the simplified classification and 3.6 for the Herbert Classification ($p < 0.05$).
**Conclusions:** All complete fractures across the entire scaphoid distal to the scapholunate articulation and proximal to the STT joint can be classified as waist fractures, non-waist scaphoid fractures are uncommon (6%) and have somewhat different presentations compared to waist fractures. Simplifying the fracture classification slightly improves inter-observer reliability, although remaining fair, and significantly reduces doubt.
**Level of Evidence:** Level III, Prognostic

## INTRODUCTION

There is a great variety of scaphoid fracture classification systems with considerable controversies. Popular classification systems include the Herbert[1] and Mayo[2] classifications, but there are many more.[1,2] All classifications have two limitations in common, they were based on standard radiographs only and their complexity hinders a satisfactory inter-observer reliability.[3] To improve comparison in the literature, there is a trend to simplify fracture classifications by dividing the bone geometrically into a proximal, waist and distal third. However, accurate classification of the involved third of the scaphoid relies on defining the longitudinal axis which requires computed tomography.

Based on three-dimensional fracture pattern analysis of xxx consecutive scaphoid fractures as presented in part one of this study, it seems that the scaphoid fracture classification can be simplified to proximal pole fractures, a range of waist fractures and tubercle avulsion fractures. It has been shown that the vast majority of fractures can be classified on posteroanterior radiographs as (1) proximal pole fractures (proximal to the distal scapholunate interval), (2) a range of waist fractures (involving the scaphocapitate interval), and (3) distal tubercle fractures (involving the scapho-trapezio-trapezoid interval).

A first purpose of this study was to analyze the reproducibility and demographics of a simplified scaphoid fracture classification using a large database of scaphoid fractures diagnosed on posteroanterior radiographs (1. database study). The secondary purpose was to test the results of a simplified scaphoid classification based on the findings of part of one of this study using an inter-observer study while comparing to the most used scaphoid fracture classification by Herbert. (2. interobserver study)



## MATERIAL AND METHODS

### 1. Database study

The institutional review board (IRB) approved this retrospective study and a waiver of informed consent was granted. We identified 2,555 consecutive patients that were diagnosed with a (suspected) scaphoid fracture between January 2003 and July 2014 based on International Classification of Diseases, 9$^{th}$ Revision, Clinical Modification (ICD-9-CM) codes 814.01 (Closed fracture of navicular [scaphoid] bone of wrist) and 814.11 (Open fracture of navicular [scaphoid] bone of wrist).

We included patients aged 18 years or older with an acute fracture (diagnosed within 30 days of injury) confirmed on radiographs or CT-scan. Posteroanterior radiographs were used to analyze the reproducibility of the simplified scaphoid fracture classification by one investigator and checked by a senior hand surgeon. Proximal pole fractures

were defined as fractures in which the center of the fracture line was proximal to the distal scapholunate interval. Waist fractures were defined as fractures involving the scaphocapitate interval. Distal tubercle fractures were defined as fractures involving the scapho-trapezio-trapezoid interval. (Figure 1) Any fracture that could not be classified by this simplified system was recorded. Demographic analysis was performed to investigate associated factors of the three types of fractures patterns.
We excluded 886 of the 2555 patients (35%) because they had no fracture (suspected scaphoid fracture) and 105 (4.1%) were excluded because they were underage at the time of diagnosis. Another 641 patients (25%) were excluded because they were diagnosed more than 30 days after injury or had an ununited fracture, eleven patients were excluded as they had their initial treatment at a different institution, and 41 (1.6%) were excluded because no radiographs were available in the medical record. The final cohort consisted of 871 (34%) scaphoid fractures.
Among our final cohort of 871 patients with an acute scaphoid fracture, all fractures could be classified as proximal pole, waist or distal tubercle fractures on posteroanterior radiographs. There were 802 (92%) waist fractures, of which 61 (7.6%) were part of a perilunate fracture dislocation. There were 30 (3.4%) proximal pole fractures and 39 (4.5 %) distal tubercle fractures (Table 2).

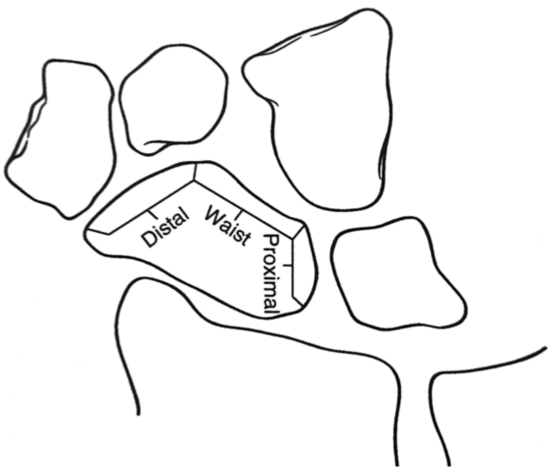



**Figure 1.** Simplified classification; distal, waist and proximal pole fractures

## 2. Interobserver study

After approval by our institutional review board, members of the Science of Variation Group (SOVG) with an interest in hand surgery or fractures were invited to participate in this study. Among the 84 surgeons that felt the study was appropriate for their expertise and interests, 72 completed the questionnaire.

Radiographs of patients with scaphoid waist fractures made 0-4 weeks after injury (CAST trial) were obtained (Buijze and Goslings et al., 2014). Relevant patients were than manually identified and assessed in the electronic medical record system, at 2 institutions. Inclusion criteria were: patients aged 18 years or older treated non-operatively for a fracture of the scaphoid waist or proximal pole.
Participants were shown radiographs of the 39 patients in posteroanterior, lateral and oblique fashion and were asked to diagnose the fracture using the Herbert classification and the simplified classification, and to indicate the doubt of their answer. We also recorded each observer's sex, location of practice, years of practice, supervision of trainees, and specialization.
The vast majority of the 72 participants were men (n=71,99%). Seventy-two percent specialized in hand and wrist surgery (n=52) and 19% in traumatology (n = 14) (Table 1). Twelve participants didn't complete the survey and were excluded from further analysis.



## Statistical Analysis
### 1. Database study
Continuous data is reported as mean with standard deviation (SD) and categorical data as frequencies and percentages. For the database study the waist fracture group was used as a reference group for the distal tubercle and proximal pole fractures. In bivariate analysis, we used a Fisher exact test to assess the association between dichotomous explanatory variables and fracture type. A Student t-test was used to test the association between continuous variables and fracture type. We analyzed the following explanatory variables: affected side, time between injury and treatment, smoking status, hospital of service, hand surgeon, hand dominance, injury type, fracture displacement, nonunion, perilunate dislocation, other wrist fractures and surgery.
Multivariable logistic regression analysis was used to assess the independent relationship of explanatory variables with the different types of scaphoid fractures by including all variables with a *P* value below 0.10 in bivariate analysis. All statistical analyses were performed using Stata® 13 (StataCorp LP, College Station, TX, USA) and a two-tailed *P* value below 0.05 was considered significant.

### 2. Interobserver Study
Continuous data is reported as mean with standard deviation (SD) and categorical data as frequencies and percentages. For the interobserver study the multi-rater kappa measure described by Siegel and Castellan[5] was used to measure interobserver agreement.5 Using the guidelines of Landis and Koch the generated kappa values were interpreted as follows: 0.01 to 0.20 defines slight agreement; 0.21 to 0.40, fair agreement; 0.41 to 0.60, moderate agreement; 0.61 to 0.80, substantial agreement; 0.81 to 0.99, almost perfect agreement and 1.00, perfect agreement. Zero indicates no agreement beyond chance alone; while –1.00 indicates total disagreement.[6]

Table 1: Observer characteristics

| **Characteristics** | **n (%)** |
|---|---|
| n=72 | |
| **Gender** | |
| men | 71 (99) |
| women | 1 (1) |
| **Location of practice** | |
| US/Canada | 48 (67) |
| Europe | 13 (18) |
| Asia | 1 (1) |
| Australia | 3 (4) |
| Other | 7 (10) |
| **Years in practice** | |
| 0 to 5 | 22 (31) |
| 6 to 10 | 15 (20) |
| 11 to 20 | 26 (36) |
| 21 to 30 | 9 (13) |
| **Supervising trainees** | |
| yes | 70 (98) |
| no | 2(2) |
| **Specialization** | |
| Hand-wrist | 52 (72) |
| Traumatolgy | 1 (1) |
| Shoulder/elbow | 14 (19) |
| Other | 5 (8) |

# RESULTS

## 1. Database study

In bivariate analysis, patients with proximal pole fractures were significantly (*P* = 0.001) younger on average, more likely to smoke (P=0.03), more often had an associated ulna styloid fracture (P=0.02) compared to patients with waist fractures (Table 2). Patients with proximal pole fracture were more likely to have a CT-scan (*P* = 0.001) and the injury was never related to sports (P=0.005). Using multivariable logistic regression analysis to account for any confounding, younger age was the only factor independently associated with proximal pole fractures compared to waist fractures (Table 3; OR 0.94, 95% CI 0.91-0.98, *P* = 0.002). Distal tubercle fractures were never related to sports either (P=0.001) and patients were much less likely to have operative treatment. (n=3; *P* < 0.001)

## 2. Inter-observer study

There was fair agreement using the Herbert classification for the scaphoid fractures ($\kappa$ =0.31; 95%CI 0.216-0.397). Agreement classification of scaphoid fractures using the simplified classification was also fair ($\kappa$ = 0.37; 95%CI 0.256-0.477). The average doubt of the answers of the observers was 2.1 on a scale from 0-10 for the simplified classification and 3.6 for the Herbert Classification, a significant difference ($p< 0.05$).

Table 2: Bivariate analysis of factors associated with proximal, distal, and waist fractures of the scaphoid (n = 871)

| | Proximal Pole | | Tubercle | | Waist (reference) |
|---|---|---|---|---|---|
| **Number (%)** | 30 (3.4%) | | 39 (4.5%) | | 802 (92%) |
| **Parameter** | **Mean (SD)** | **P-value*** | **Mean (SD)** | **P-value*** | **Mean (SD)** |
| **Age, years** | 28 (9.7) | 0.001 | 38 (21) | 0.83 | 39 (19) |
| **Time to treatment, days** | 1.5 (3.5) | 0.24 | 3.2 (5.7) | 0.59 | 2.7 (5.4) |
| | **Number (%)** | **P-value** | **Number (%)** | **P-value** | **Number (%)** |
| **Sex** | | | | | |
| Men | 25 (83%) | 0.22 | 29 (74%) | 0.72 | 570 (71%) |
| Women | 5 (17%) | | 10 (26%) | | 232 (29%) |
| **Smoking** ** | *n = 27* | | *n = 31* | | *n = 649* |
| Never | 19 (70%) | | 24 (77%) | | 421 (65%) |
| Current | 8 (30%) | **0.03** | 3 (10%) | 0.38 | 125 (19%) |
| Former | 0 | | 4 (13%) | | 103 (16%) |
| **Race** | | | | | |
| White | 23 (77%) | 0.99 | 31 (79%) | 0.85 | 619 (77%) |
| Other | 7 (23%) | | 8 (21%) | | 183 (23%) |
| **Hand surgeon** | *n = 29* | | *n = 39* | | *n = 790* |
| | 19 (66%) | 0.19 | 28 (72%) | 0.57 | 600 (76%) |
| **Affected side right** | | | | | |
| | 12 (40%) | 0.85 | 18 (46%) | 0.74 | 343 (43%) |
| **Injury Type** | | | | | n = 794 |
| Trauma | 30 (100%) | **0.005** | 37 (95%) | **0.001** | 613 (77%) |
| Sports | 0 | | 2 (5.1%) | | 181 (23%) |
| **CT** | | | | | |
| CT scan | 20 (67%) | **0.001** | 16 (41%) | 0.50 | 287 (36%) |
| **Perilunate dislocation** | | | | | |
| | 0 | 0.16 | 1 (2.6%) | 0.35 | 61 (7.6%) |
| **Isolated fracture** | | | | | |
| Isolated fracture | 19 (63%) | 0.07 | 29 (74%) | 0.55 | 629 (78%) |
| Distal radius | 8 (27%) | 0.14 | 4 (10%) | 0.38 | 113 (17%) |
| Capitate | 0 | 0.99 | 0 | 0.99 | 12 (1.5%) |
| Hamate | 1 (3.3%) | 0.33 | 1 (2.6%) | 0.41 | 10 (1.3%) |
| Lunate | 1 (3.3%) | 0.52 | 1 (2.6%) | 0.61 | 19 (2.4%) |
| Trapezium | 0 | 0.99 | 0 | 0.99 | 10 (1.3%) |
| Triquetrum | 1 (3.3%) | 0.99 | 1 (2.6%) | 0.99 | 29 (3.6%) |
| Ulna | 5 (17%) | **0.02** | 4 (10%) | 0.15 | 41 (5.1%) |
| **Operative treatment** | | | | | |
| | 16 (53%) | 0.09 | 3 (7.7%) | **< 0.001** | 300 (37%) |

SD = standard deviation, * Compared to waist group, ** according to the medical records

Table 3: Multipele logistic regression comparing scaphoid waist and proximal pole fractures

| | Waist- Proximal Pole (n=831) | |
|---|---|---|
| | **Odds ratio (95% CI)** | **P-value** |
| **Age** | 0.94 (0.91 - 0.98) | **0.001** |
| **Smoking** | 1.8 (0.74 - 4.1) | 0.20 |
| **Isolated fracture** | 0.54 (0.21 - 1.4) | 0.20 |
| **Other fractures** | | |
| Ulna | 3.3 (0.94 - 12) | 0.063 |

## DISCUSSION

To improve comparison of studies on scaphoid fractures, it is crucial to develop a simple and reproducible classification system. This study shows that the simplifying scaphoid fractures classification into proximal pole, waist or distal tubercle fractures was easily reproducible in a large series and fractures that do not fit this classification are rare. [see part one of this article] We were able to successfully classify all fractures in our retrospective review group using the simplified classification. Our inter-observer study compared the simple classification with the Herbert classification and showed fair agreement for both classifications but significantly less doubt when classifying scaphoid fractures using the simplified classification.

There is evidence that most fractures are waist fractures and the appearance of being relatively distal or proximal may often be an artifact of how these fractures project on radiographs.[7] If one includes relatively distal fractures that cross the entire scaphoid as (distal) waist fractures, waist fractures account for more than 90% of all scaphoid fractures. This is slightly higher than previously reported using different classifications. For example, Grewal et al reviewed 219 scaphoid fractures over a 6-year period and found that 28 (13%) involved the proximal pole, 18 (8%) the distal pole, and 173 (79%) the waist according to the classification of Herbert.[8]

This study has several limitations. First, the retrospective design did not account for all potential factors associated with the different fracture types. Second, the relatively low number of proximal pole (n = 30) and distal tubercle fractures (n=39) hindered multivariable statistical analysis. A larger sample with more proximal pole and distal tubercle fractures might have resulted in more statistical power to detect subtle but relevant differences between different fracture types. In this manuscript only the distal tubercle fractures are classified to be fractures located distal. Using the suggested new (simplified) classification it seems easy to classify the different type of fractures.

Defined into three categories as we did in a prior fracture pattern analysis, we found a greater percentage of waist fractures is greater in study than in prior studies. It shows that this fits our experience. In part one of this study, we have shown that from a 3D perspective of scaphoid fractures there seems to be a wide distribution of waist fractures and only a small amount of proximal scaphoid fractures. Attempts to study distal tubercle fractures and proximal pole fractures are hindered by the relative infrequency of these injuries and the difficulty deciding which fractures count as proximal pole fractures. A study to look at the reliability of diagnosis of proximal pole versus waist fractures is currently being performed.[9]

When classifying scaphoid fractures in the three groups as described there might only be some rare exceptions. Slutsky *et al*. described a series of 6 cases with coronal fractures which wouldn't fit our classification, but neither would it fit any other classification.[10] The same is true for horizontal oblique fracture running through the tubercle at the scaphocapitate interval. Oron *et al* described different types of distal pole fractures in a case series of 7. Their cases were not only situated in the distal tubercle and could neither be classified as a distal waist fracture.[11] We do not want to imply that this type of distal pole factures (other than distal tubercle fractures) do not exist but we think that they are so rare and therefore not seen in our series.

In 1993 Compson *et al* described three cases of avulsion fractures and concluded that they are rarely reported in literature, that their cases appear to be identical arising from the dorsal ridge of the scaphoid.[12] In 2016 Luria *et al* found similar results in a 3D imaging study by taking a closer look at the fracture location (using the Herbert classification), as the manuscript was mainly on fracture angles. In their population they had a number of distal tubercle fractures, all located very distally involving the distal tubercle and for the most part fractures were located in the waist. This is consistent with our theory that distal scaphoid fractures are through the tubercle.[13] Brondum *et al* used the Russe classification to describe their population of scaphoid fractures in Denmark and found an incidence of 5 patients suffering from an avulsion or tubercle of the scaphoid per 100000 inhabitants. They also showed that there is a wide distribution in numbers of patients reported suffering from scaphoid fractures when subdivided into 3 groups (proximal, mid and distal). It varied from only 15% classified as mid-scaphoid fracture and 85% distally located to 86% mid, 9% distal and 5% proximal location in the scaphoid.[14,15] The interobserver study shows fair agreement for the simplified classification and also for the Herbert classification and no significant difference. Using the simplified classification observers have less doubt when classifying the scaphoid fractures compared to the Herbert classification.

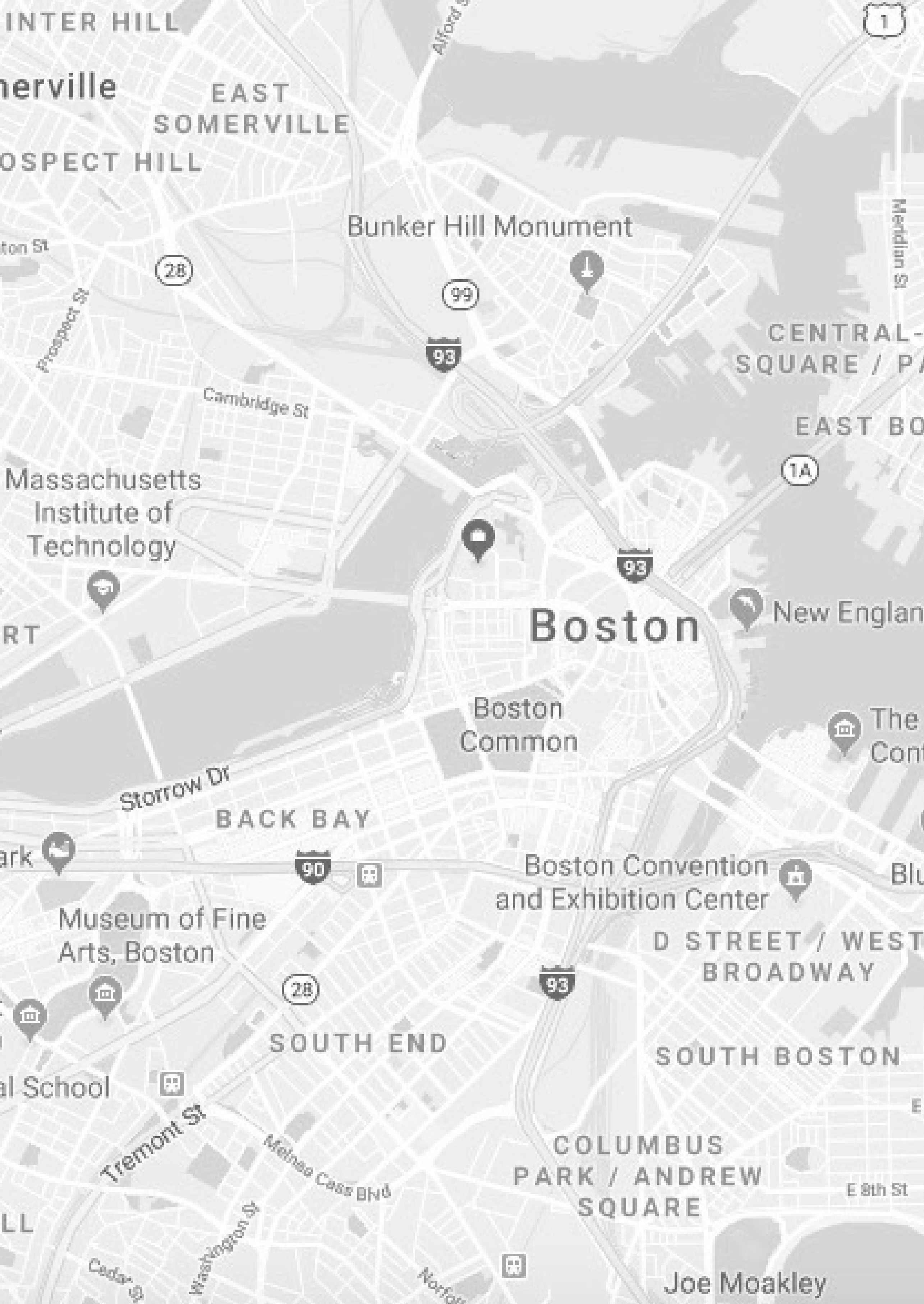
In conclusion, when we defined waist fractures as distal to the scapholunate articulation and proximal to the STT joint, our retrospective review found non-waist, scaphoid fractures are uncommon (6%). Further investigation using an even larger multi-institutional database to incorporate more proximal pole and tubercle fractures may be necessary to study the epidemiology of these fractures more accurately.

## REFERENCES


1. Herbert TJ, Fisher WE. Management of the fractured scaphoid using a new bone screw. *J Bone Joint Surg Br*. 1984;66(1):114-123
2. Cooney WP, Dobyns JH, Linscheid RL. Fractures of the scaphoid: a rational approach to management. *Clin Orthop Relat Res*. 1980(149):90-97
3. Ten Berg PW, Drijkoningen T, Strackee SD, Buijze GA.J Classifications of Acute Scaphoid Fractures: A Systematic Literature *ReviewWrist Surg*. 2016 May;5(2):152-9. doi: 10.1055/s-0036-1571280.
4. Buijze GA, Goslings JC, Rhemrev SJ, Weening AA, Van Dijkman B, Doornberg JN, Ring D; CAST-Trial Collaboration.Cast immobilization with and without immobilization of the thumb for nondisplaced and minimally displaced scaphoid waist fractures: a multicenter, randomized, controlled trial. J Hand Surg Am. 2014 Apr;39(4):621-7. doi: 10.1016/j.jhsa.2013.12.039. Epub 2014 Feb 28.
5. Siegel S CJ. Nonparametric Statistics for the Behavioral Sciences. 2nd Edn. New York, McGraw-Hill, 1988.
6. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics. 1977, 33: 159-74.
7. Compson JP. The anatomy of acute scaphoid fractures: a three-dimensional analysis of patterns. *J Bone Joint Surg Br*. 1998 Mar;80(2):218-224.
8. Grewal R, Suh N, Macdermid JC. Use of computed tomography to predict union and time to union in acute scaphoid fractures treated nonoperatively. *J Hand Surg Am*. 2013;38(5):872-877
9. Beks RB, Drijkoningen T, Claessen F, Guitton TG, Ring D; Science of Variation Group. Interobserver Variability of the Diagnosis of Scaphoid Proximal Pole Fractures. J Wrist Surg. 2018 Sep;7(4):350-354. doi: 10.1055/s-0038-1641716.
10. Slutsky DJ, Herzberg G, Shin AY, Buijze GA, Ring DC, Mudgal CS, Leung YF, Dumontier C. Coronal Fractures of the Scaphoid: A Review. *J Wrist Surg*. 2016 Aug;5(3):194-201. doi: 10.1055/s-0036-1585414.
11. Oron A, Gupta A, Thirkannad S. Nonunion of the scaphoid distal pole. *Hand Surg*. 2013;18(1):35-39. doi: 10.1142/S0218810413500068.
12. Compson JP, Waterman JK, Spencer JD. Dorsal avulsion fractures of the scaphoid: diagnostic implications and applied anatomy. *J Hand Surg Br*. 1993 Feb;18(1):58-61.
13. Luria S, Schwarcz Y, Wollstein R, Emelife P, Zinger G, Peleg E.3-dimensional analysis of scaphoid fracture angle morphology. *J Hand Surg Am*. 2015 Mar;40(3):508-514. doi: 10.1016/j.jhsa.2014.11.008.
14. Mttssbichler H. Injuries of the carpal scaphoid in children. *Acta Radio1* 1961; 56: 361-368.
15. Schemberg F. Classification of fractures of the carpal scaphoid. An anatomo-radiologic study of characteristics. *Rev Chir Orthop* 1988; 74: 693-695.

# PART III

## PHYSICIAN INTERPRETATION OF DIAGNOSTICS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Tremont St
Melnea Cass Blvd
COLUMBUS PARK / ANDREW SQUARE
E 8th St
Washington St
Joe Moakley

# Chapter 5

## Interobserver variability in diagnosis of scaphoid proximal pole fractures

Journal of Wrist Surgery, 2018
Beks RB, **Drijkoningen T**, Claessen F, Guitton TG, Ring D; Science of Variation Group

# Abstract

**Purpose**: Fractures of the proximal pole of the scaphoid are prone to adverse outcomes such as nonunion and avascular necrosis. Distinction of scaphoid proximal pole fractures from waist fractures is important for management but it is unclear if the distinction is reliable.

**Methods**: A consecutive series of 29 scaphoid fractures from one tertiary hospital was collected consisting of five scaphoid proximal pole and 24 scaphoid waist fractures. Fifty-seven members of the Science of Variation Group (SOVG) were randomized to diagnose fracture location and displacement of using radiographs alone or radiographs and a CT-scan.

**Results**: Observers reviewing radiographs alone and observers reviewing radiographs and CT-scans both had substantial agreement on fracture location ($\kappa = 0.82$ and $\kappa = 0.80$, respectively; $p = 0.54$). Both groups had only fair agreement on fracture displacement, ($\kappa = 0.28$ and $\kappa = 0.35$, respectively; $p = 0.029$).

**Conclusion**: Proximal pole fractures are sufficiently distinct from proximal waist fractures that computed tomography does not improve reliability of diagnosis.

## INTRODUCTION

Fractures of the proximal pole of the scaphoid are prone to adverse outcomes, such as nonunion and avascular necrosis.[1–4] Operative treatment is more readily considered for proximal pole fractures than for waist fractures.[5] The data regarding the management of proximal pole fractures may be clouded by imprecision in distinction of waist fractures from proximal pole fractures. Relatively few scaphoid fracture classification systems describe how to distinguish proximal pole and scaphoid waist fractures. (Table 1). Given the strong association between fracture displacement and nonunion for scaphoid waist fractures it is also important to identify whether the fracture is displaced or not.[6,7] We know little about the accuracy and reliability of imaging methods to identify fracture displacement of proximal pole scaphoid fractures. Lozano- Calderon et al. concluded that an additional CT scan improves the reliability of diagnosis of scaphoid displacement compared to radiographs alone.[8] Buijze et al. showed that radiographs and computed tomography (CT) scans did not accurately identify fracture displacement of scaphoid waist fractures.[6] They also found that the interobserver reliability was poor and improved only slightly with training.[9] This study tested the primary null hypothesis that there is no difference in interobserver agreement for the diagnosis of proximal pole fractures of the scaphoid between observers that view radiographs alone and those that review radiographs and CT scans. It also addressed the secondary null hypothesis that there is no difference for the identification of fracture displacement.

5

**Table 1: Fractures of the scaphoid based on fracture location**

| Author (year) | Cases | Type Fracture | Definition proximal pole |
|---|---|---|---|
| Cooney (Mayo; 1980) | 45 | 1 Tuberosity<br>2 Distal articular surface<br>3 Distal one-third<br>4 Waist, middle one-third<br>5 Proximal pole | Proximal third on PA radiograph |
| Schernberg (1984) | 325 | I Proximal pole<br>II, III, IV Waist<br>V Distal Pole<br>VI- a,b,c Distal tubercle | Involving about a third of the articular surface of the scaphoid with the radius and exiting at the capitolunate articulation. |
| AO/OTA (2007) | - | A1 Proximal pole, noncomminuted<br>A2 Waist, noncomminuted<br>A3 Distal pole, noncomminuted<br>B2 Waist, comminuted | Not clearly described |
| Herbert/Modified Herbert (1984/1996) | 200/431 | A1 Stable, Tubercle<br>A2 Stable, Incomplete waist<br>B1 Unstable, Distal oblique<br>B2 Unstable, Complete waist<br>B3 Unstable, Proximal pole<br>B4 Unstable fracture dislocation<br>B5 Unstable, Comminuted | Not clearly described |

## METHODS

After approval of our institutional review board, members of the Science of Variation Group (SOVG; 377 upper extremity surgeons) were invited to participate in this study. Of these, 84 (22%) surgeons responded and 57 (15%) completed the questionnaire. This is not a response rate since the email list of SOVG participants is not updated or filtered. Invitations were sent via email in December 2015, followed by a reminder 10 days later. The SOVG is an international collaboration of orthopaedic surgeons with upper extremity specialization. The aim of the collaboration is to study variation in definition, in this case scaphoid fracture location, and treatment of illness without financial incentives.

CT-scans and radiographs of both patients with scaphoid proximal pole fractures and scaphoid waist fractures were obtained from a multi-institutional Research Patient Data Registry (RPDR) in a period from 2003-2015. RPDR is a centralized clinical data registry holding diagnostic codes (International Classification of Diseases, 9th revision code), Current Procedural Terminology (CPT) codes, demographic information (e.g. sex, date of birth, and race), radiology and operative reports, and visit notes.

Inclusion criteria were: patients of 18 years or older, availability of scaphoid radiograph series (posteroanterior wrist with ulnar deviation, lateral wrist, oblique wrist, and a scaphoid view [20-30 degrees tube angle]) and a CT scan that could be reformatted in the planes defined by the long axis of the scaphoid.[10] To obtain a sufficient number of patients with a proximal pole fracture, a CT scan and to have a representative series, a consecutive series of scaphoid fractures was obtained until there were five scaphoid proximal pole fractures. This resulted in 29 scaphoid fractures of which five were proximal pole fractures, identified by consensus between a radiologist and a hand surgeon without the use of a classification.

For this study participants of the SOVG were divided in two groups at random. Using SurveyMonkey (Palo Alto, CA, USA), participants were asked to decide on a diagnosis and displacement of either a waist or a proximal pole fracture, using radiographs alone or radiographs and a CT-scan. No training, guidance, or measurement was provided in order to test what surgeons do in their daily practice.

The following explanatory variables were obtained: sex of observer, location of practice, years of practice, specialization of observer.

### Statistical Analysis

The multirater kappa measure described by Siegel and Castellan[11] was used to determine interobserver agreement. Using the guidelines of Landis and Koch the generated kappa values were interpreted where a value of: 0.01 to 0.20 defines slight agreement; 0.21 to 0.40, fair agreement; 0.41 to 0.60, moderate agreement; 0.61 to 0.80, substantial agreement; and 0.81 to 0.99, almost perfect agreement and 1.00, perfect agreement.

Zero indicates no agreement beyond chance alone; –1.00, total disagreement.[12] A two-sample z test was used to compare kappa values and P values of <0.05 were considered significant.

## Observer characteristics

The majority of the 57 participants were men (n = 52, 91%) and practiced in the United States of America (n = 43, 75%) (Table 2). Most participants specialized in orthopaedic traumatology (n = 40, 70%) and supervised trainees in the operating room (n = 51, 89%).

Table 2: Observer Demographics (n=57)

| **Demographic** | **Radiographs N (%)** | **Radiographs plus CT N (%)** | **Total N** |
|---|---|---|---|
| Sex | | | |
| Male | 27 (100) | 25 (83) | 52 |
| Female | 0 | 5 (17) | 5 |
| Area | | | |
| United States | 17 (63) | 26 (87) | 43 |
| Europe | 6 (22) | 3 (10) | 9 |
| Other | 4 (15) | 1 (3) | 5 |
| Years in independent practice | | | |
| 0-5 | 9 (33) | 10 (33) | 19 |
| 6-10 | 8 (30) | 4 (13) | 12 |
| 11-20 | 8 (30) | 13 (43) | 21 |
| 21-30 | 2 (7) | 3 (10) | 5 |
| Specialization | | | |
| Traumatology | 20 (74) | 20 (67) | 40 |
| Shoulder and elbow | 2 (7) | 5 (17) | 7 |
| Hand and wrist | 5 (19) | 5 (17) | 10 |
| Supervises trainees in the operating room | | | |
| Yes | 24 (89) | 27 (90) | 51 |
| No | 3 (11) | 3 (10) | 6 |

## RESULTS

Observers reviewing radiographs alone and observers reviewing radiographs and CT-scans had substantial agreement on fracture location (κ = 0.82 and κ = 0.80, respectively; p = 0.53) (Table 3). Both groups had only fair agreement on fracture displacement, but the kappa value was significantly lower in the group reviewing radiographs and CT-scans compared to those reviewing radiographs alone (κ = 0.28 and κ = 0.35, respectively; *p* = 0.029) (Table 3).

Table 3: Overall Interobserver Agreement

| | Radiographs | | | | Radiographs plus CT-scan | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Question** | **κ** | **SE** | **Agreement** | **95% CI*** | **κ** | **SE** | **Agreement** | **95% CI*** | **P value** |
| Is it a scaphoid proximal pole or waist fracture? | 0.82 | 0.0269 | almost perfect | 0.76 - 0.87 | 0.80 | 0.0186 | substantial | 0.76 - 0.83 | 0.532 |
| Is the fracture displaced? | 0.35 | 0.0119 | fair | 0.32 - 0.37 | 0.28 | 0.0288 | fair | 0.22 - 0.34 | **0.034** |

*SE = Standard Error. CI = confidence interval; CI calculated (κ- [1.96 x SEM], κ + [1.96 x SEM]; κ = Cohen's kappa coefficient

## DISCUSSION

Since scaphoid fracture treatment is based in part on location, reliable diagnosis of fracture location and displacement are important. This study compared the reliability of diagnosis of scaphoid fracture location and displacement using radiographs alone versus radiographs and CT scans. CT scans did not have a meaningful influence on the reliability of diagnosis on average. The diagnosis of displacement is unreliable.

This study has several limitations. First, the fractures were retrieved from a single tertiary hospital, which could limit generalizability, although that seems unlikely. Second, our results could be subject to a spectrum bias since proximal pole fractures were over represented in our sample. Third, most SOVG participants work in an academic setting (90% supervises trainees) and their values, training, and practice might differ from the larger community of surgeons. Fourth, there is no consensus definition of scaphoid proximal pole fractures and we did not use any training.[13] An advantage is that the study reflects daily clinical practice. A subset of observers might change their judgment when viewing radiographs and CT scans in the typical fashion. Finally, in this study—as in all Science of Variation Group studies we did not assess intraobserver variability because it

is always greater than interobserver variability and it's more difficult to study.
There was no difference in agreement on diagnosis of scaphoid fracture location with the use of either radiographs alone or when radiographs were accompanied by a CT-scan. The reliability was high for both. This suggests that proximal pole scaphoid fractures are sufficiently distinct from waist fractures that the added detail provided by computed tomography does not improve the reliability of diagnosis of fracture location.
In contrast, diagnosis of fracture displacement was only fair, with computed tomography providing no advantage. Lozano-Calderon et al studied the reliability of diagnosis of fracture displacement of 30 scaphoid fractures among 6 observers with arthroscopy as the reference standard demonstrated a reliability in kappa values of 0.43 for CT alone, 0.48 for CT and radiography, and 0.27 for observers just using radiographs; the average accuracy was 68%, 77%, and 75%, respectively.[8] Buijze et al studied displacement in 44 scaphoid waist fractures based on radiographs and CT scans, and also used arthroscopy as the reference standard.[6] They found that radiographs had an accuracy of 70 % and CT scans of 82% for fracture displacement diagnosis when compared with arthroscopic examination. The study of Bernard et al found diagnosis of displacement had an estimated overall accuracy of 72% using conventional radiography in cadaver study with artificially created scaphoid waist fractures. Of the 90 total possible pairwise agreements between interpreters regarding fracture displacement, there were 54 actual agreements (60%) with a kappa of 0.31 indicating fair interobserver agreement.[14] Collectively these studies suggest that CT scans are useful for ruling out displacement, but cannot reliably or accurately diagnose the presence of displacement.
The current study suggests that computed tomography does not meaningfully improve the reliability of diagnosis of fracture location (which was almost perfect) or displacement (which was fair) in the scaphoid waist and proximal pole. Future studies might address dynamic imaging such as fluoroscopy or the impact of training and clear definitions of specific fracture types and displacement. It may be that proximal pole fractures are sufficiently distinct from proximal waist fractures that sophisticated imaging is unnecessary.

# Legend

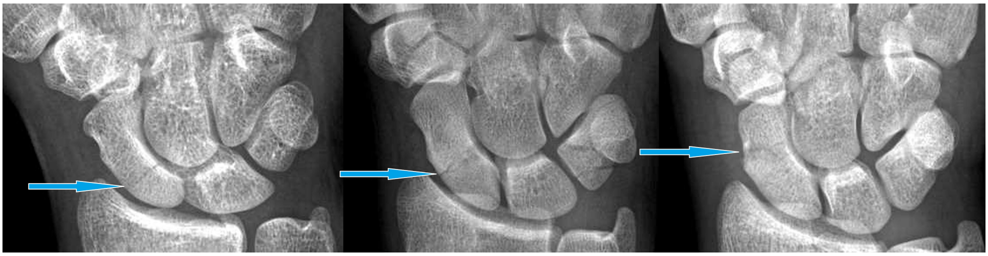

**Figure 1.** Anterior-posterior radiographs showing scaphoid fractures. Fractures are indicated with an arrow. Left: scaphoid proximal pole fracture, rated as proximal pole by 89% of observers and as a waist fracture by 11%; middle: scaphoid waist fracture where most interobserver variability was seen, rated as proximal pole by 23% of observers and as waist fracture by 77%; right: scaphoid waist fracture, rated as scaphoid waist fracture by all observers.

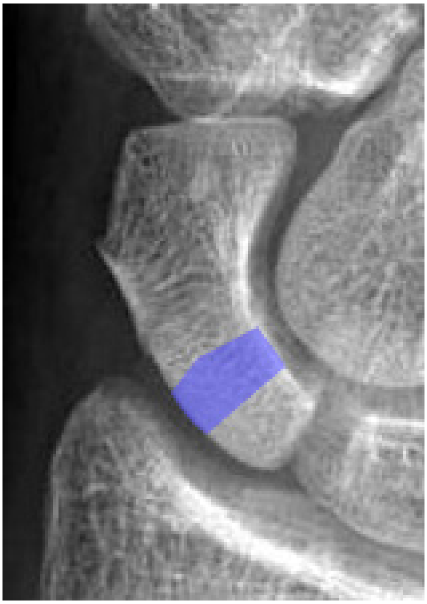

**Figure 2.** Anterior-posterior radiograph indicating of the scaphoid indicating the fracture zone where the distinction of proximal pole and waist fractures was less reliable.

## References


1. Buijze GA, Ochtman L, Ring D. Management of scaphoid nonunion. *J Hand Surg Am*. 2012;37(5):1095-100; quiz 1101. doi:10.1016/j.jhsa.2012.03.002.
2. Krimmer H. Management of acute fractures and nonunions of the proximal pole of the scaphoid. *J Hand Surg Br*. 2002;27(3):245-248. doi:10.1054/jhsb.2001.0736.
3. Ring D, Jupiter JB, Herndon JH. Acute fractures of the scaphoid. *J Am Acad Orthop Surg*. 2000;8(4):225-231. http://www.ncbi.nlm.nih.gov/pubmed/10951111.
4. Szabo RM, Manske D. Displaced fractures of the scaphoid. *Clin Orthop Relat Res*. 1988;(230):30-38. http://www.ncbi.nlm.nih.gov/pubmed/3284681.
5. Adams JE, Steinmann SP. Acute scaphoid fractures. *Orthop Clin North Am*. 2007;38(2):229-35, vi. doi:10.1016/j.ocl.2007.02.004.
6. Buijze GA, Jorgsholm P, Thomsen NO, Bjorkman A, Besjakov J, Ring D. Diagnostic performance of radiographs and computed tomography for displacement and instability of acute scaphoid waist fractures. *J Bone Jt Surg Am*. 2012;94(21):1967-1974. doi:10.2106/JBJS.K.00993.
7. Singh HP, Taub N, Dias JJ. Management of displaced fractures of the waist of the scaphoid: meta-analyses of comparative studies. *Injury*. 2012;43(6):933-939. doi:10.1016/j.injury.2012.02.012.
8. Lozano-Calderon S, Blazar P, Zurakowski D, Lee SG, Ring D. Diagnosis of scaphoid fracture displacement with radiography and computed tomography. *J Bone Jt Surg Am*. 2006;88(12):2695-2703. doi:10.2106/JBJS.E.01211.
9. Buijze GA, Guitton TG, van Dijk CN, Ring D, Science of Variation G. Training improves interobserver reliability for the diagnosis of scaphoid fracture displacement. *Clin Orthop Relat Res*. 2012;470(7):2029-2034. doi:10.1007/s11999-012-2260-4.
10. Sanders WE. Evaluation of the humpback scaphoid by computed tomography in the longitudinal axial plane of the scaphoid. *J Hand Surg Am*. 1988;13(2):182-187. http://www.ncbi.nlm.nih.gov/pubmed/3351239.
11. Siegel S CJN. *Nonparametric Statistics for the Behavioral Sciences*. Vol 2nd. New York: McGraw-Hill; 1988.
12. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics*. 1977;33(1):159-174. http://www.ncbi.nlm.nih.gov/pubmed/843571.
13. Ten Berg PW, Drijkoningen T, Strackee SD, Buijze GA. Classifications of Acute Scaphoid Fractures: A Systematic Literature Review. *J Wrist Surg*. 2016;5(2):152-159. doi:10.1055/s-0036-1571280.
14. Bernard SA, Murray PM, Heckman MG. Validity of conventional radiography in determining scaphoid waist fracture displacement. *J Orthop Trauma*. 2010;24(7):448-451. doi:10.1097/BOT.0b013e3181c3e865.


Emer-Noord
Krogten
BREDA NOORD
Backer en Ruebweg
BELCRUM
Emer-Zuid
Westerparklaan
Lunetstraat
Tramsingel
BREDA CENTRUM
Ettensebaan
Wilhelminasingel
Julianalaan
PRINCENHAGE
BOEIMEER
HEUVEL
Breda
Ruitersbosch
Graaf Engelbertlaan
Mark
Bouvignelaan
Mark

# Chapter 6

## Reliability of Diagnosis of Partial Union of Scaphoid Waist Fractures on Computed Tomography

Journal of Hand and Microsurgery, 2018
**Drijkoningen T**, Ten Berg PWL, Guitton TG, Ring D, Mudgal CS

Abstract

**Purpose**: Computed tomography (CT) is increasingly used not just to diagnose union, but also to estimate the percentage of the fracture gap that is bridged by healing bone. This study tested the primary null hypothesis that there is no agreement between observers on the extent of union of a scaphoid waist fracture on computed tomography.
**Methods:** CT scans of 13 nondisplaced scaphoid waist fractures treated nonoperatively were rated by 145 observers. CT scans were done 10 to 12 weeks after injury. Observers were asked to 'eyeball' measure percentage of union.
**Results:** We found that there was a moderate agreement on the categorical degree of partial union of a scaphoid waist fracture on computed tomography ($\kappa = 0.47$; 95% CI: 0.43 - 0.52). Agreement on the location of bony bridging was slight ($\kappa = 0.14$; 95% CI: 0.09 - 0.21).
**Conclusion:** We concluded there is limited reliability of diagnosis of partial union of a scaphoid waist fracture on computed tomography and that this should be taken into account in both patient care and research.

## INTRODUCTION

Scaphoid waist fractures can result in non-union. Radiographs are often used to diagnose union and some surgeons may prolong cast immobilization based on radiographic findings. Dias and colleagues demonstrated that radiographs are not reliable for diagnosis of union.[1]

Computed tomography is increasingly used not just to diagnose union, but also to estimate the percentage of the fracture gap that is bridged by healing bone. Singh et al [2] categorized partial union of a fracture of the scaphoid waist into percentage union ranges as follows: 0% to 24%, 25% to 49%, 50% to 74%, and 75% to 99% union. Prior research suggested that computed tomography can be used to identify certain features related to non-union or prolonged union time of a scaphoid fracture.[3] Moreover, the concept of percent union on CT scans is often used in studies of scaphoid waist fractures.

This study tested the primary null hypothesis that there is no agreement between observers on the extent of union of a scaphoid waist fracture on computed tomography.

## METHODS



After approval by our institutional review board, members of the Science of Variation Group (SOVG) with an interest in hand surgery or fractures were invited to participate in this study. Among the 150 surgeons that felt the study was appropriate for their expertise and interests, 145 completed the questionnaire.

CT-scans of patients with scaphoid waist fractures made 10 to 12 weeks after injury (per the routine practice of one surgeon - CSM) were obtained by using billing codes via a research fracture database. Relevant patients were than manually identified and assessed in the electronic medical record system, at our institution. Inclusion criteria were: patients aged 18 years or older treated non-operatively for a non-displaced fracture of the scaphoid waist. All scaphoid CT scans had a slice thickness of 1.25 mm or less. All scans were made in the plane of the scaphoid. We chose waist fractures, as they are the most common type of scaphoid fracture treated by surgeons involved in fracture care. In addition, the SOVG consists of members from various subspecialties. Choosing the waist fracture allowed us to include a larger cohort of respondents who were familiar with interpretation of a scaphoid CT scan.

Participants were shown windowed videos of the 13 CT scans in coronal and sagittal fashion and were asked to diagnose the percentage bony bridging and the location of the bony bridging, and to indicate the doubt of their answer. The percentage of bony bridging was categorized according to Singh *et al.* [2] (0%; 1-24%; 25-49%, 50-74%, 75-99%, 100%). Participants were informed of this measurement technique, and were asked to 'eyeball' their measurement percentages. The location of the bony bridging was divided into anatomic areas, which included dorsal, volar, radial an ulnar. All scans were viewed on the observers' monitors and there was no restriction of time allowed to view each video. Videos could be viewed more than once. We also recorded each observer's sex, location of practice, years of practice, supervision of trainees, and specialization.

## Observer characteristics

The vast majority of the 150 participants were men (n = 144, 96%). Thirty-eight percent specialized in hand and wrist surgery (n=57) and 36% in traumatology (n = 54) (Table 1). Five participants didn't complete the survey and were excluded from further analysis.

Table 1: Characteristics of observers (n=150)

| **Gender** | |
|---|---|
| Male | 144 |
| Female | 6 |
| **Location of practice** | |
| US/Canada | 75 |
| Europe | 57 |
| Asia | 3 |
| Australia | 6 |
| Other | 9 |
| **Years in practice** | |
| 0 to 5 | 58 |
| 6 to 10 | 31 |
| 11 to 20 | 44 |
| 21 to 30 | 17 |
| **Supervising trainees** | |
| Yes | 132 |
| No | 18 |
| **Specialization** | |
| Hand-wrist | 57 |
| Traumatolgy | 54 |
| Shoulder/elbow | 19 |
| General orthopedics | 9 |
| Other | 11 |

### Statistical Analysis

The multi-rater kappa measure described by Siegel and Castellan[4] was used to measure interobserver agreement. Using the guidelines of Landis and Koch[5] the generated kappa values were interpreted as follows: 0.01 to 0.20 defines slight agreement; 0.21 to 0.40, fair agreement; 0.41 to 0.60, moderate agreement; 0.61 to 0.80, substantial agreement; 0.81 to 0.99, almost perfect agreement and 1.00, perfect agreement. Zero indicates no agreement beyond chance alone; while –1.00 indicates total disagreement.

## RESULTS

The mean amount of scaphoid fractures treated by the observers on a yearly basis was 2.7. All of the observers treated at least 1 scaphoid fracture a year and 3 surgeons treated 5 scaphoid fractures per year. There was moderate agreement on the categorical degree of partial union of a scaphoid waist fracture on computed tomography ($\kappa = 0.47$; 95% CI: 0.43 - 0.52). Agreement on the location of bony bridging was slight ($\kappa = 0.14$; 95% CI: 0.09 - 0.21) (Table 2). The average doubt of the answers of the observers was 3.8 on a scale from 0-10. (0=no doubt and 10=really in doubt)

Table 2: Inter-observer agreement (N=145)

| | **Bony bridging** | | **Location bony bridge** | |
|---|---|---|---|---|
| | Kappa | Agreement | Kappa | Agreement |
| **Overall** | 0.34 | fair | 0.31 | fair |
| **Area** | | | | |
| United States | 0.35 | fair | 0.31 | fair |
| Europe | 0.33 | fair | 0.33 | fair |
| Other | 0.36 | fair | 0.32 | fair |
| **Years in independent practice** | | | | |
| 0-5 | 0.34 | fair | 0.30 | fair |
| More than 5 years | 0.34 | fair | 0.32 | fair |

## DISCUSSION

Measuring percentage of union on a CT-scan could be helpful in studying and treating scaphoid waist fractures. To be useful this diagnostic test must be sufficiently reliable and accurate. This study measured the reliability of diagnosis of percent union on computed tomography of healing scaphoid waist fractures.

This study has several limitations. First, all cases were retrieved from a single surgeon's practice which might have caused a selection bias, although this is unlikely because we used a consecutive series of non-operatively treated non-displaced scaphoid waist fractures. Second, most SOVG participants work in an academic setting (82% supervise trainees) and their values, training, and practice might differ from the larger community of surgeons. Third, images were presented in a standardized fashion, which did not allow observers to adjust and manipulate images as would be the case in their daily practice. However, a study found the format of imaging visualization, has limited influence on interpretation.[6] We asked the observers to 'eyeball' measure the percentage and location of bony bridging, without giving them further instructions. The purpose was to make the study resemble actual clinical situations, across a spectrum of surgeons' practice settings. While this might have caused some uncertainty in the answers, it does show the wide variability in interpretation of CT scans in scaphoid fractures.

Surgeon reliability of diagnosis of partial union is moderate. This is consistent with the evidence that diagnosis of scaphoid fracture characteristics on radiological images has limitations. For instance, in one study 2 observers rated 151 scaphoid waist fractures on radiographs and measured fair to moderate agreement on the Herbert, Russe, and Compson classifications, as well as diagnosis of fracture comminution, displacement, and the fracture location.[7] In the last decade, CT-scans have become more popular in the management of scaphoid fractures. In one study, 66 patients had a CT scan of the scaphoid 12-18 weeks after an acute scaphoid fracture treated in a below elbow cast for 8 to 12 weeks; 14 fractures did not show any evidence of union, 30 had union across the entire fracture, and 22 were partially united. A study of CT diagnosis of union by 3 observers of 48 patients with a scaphoid waist fracture found moderate inter-observer agreement ($\kappa$=0.58).[8] A study of the reliability and accuracy of diagnosis of union on CT scans among 59 raters found substantial reliability, but a negative predictive value of 0.41 (0-0.84) and a positive predictive value of 0.99 (0.97-1), indicating that CT scans are reliable for diagnosis of union but inadequate for ruling out non-union of scaphoid waist fractures between 6 and 10 weeks after injury.[9]

Agreement on the location of a healing bridge was slight. This is likely due to adding the unreliability of diagnosing union to the unreliability of determining the location of healing.

We found raters to be doubtful of their responses to some extent. It is quite possible that this could be due to low confidence in diagnosing the location of bony bridging and in the ability to quantify the percentage of bony bridging. We can speculate that we might have found a better confidence among the raters if we had simply asked if the raters thought whether there was or there was not bony bridging. Furthermore, our speculation would extend to a better confidence among raters if we had asked whether bony bridging was more or less than 50% (2 categories).

We do think that quantifying degree of bony bridging may have an impact on treatment. If there is only 0-24% bony bridging after 6-10 weeks of non-operative treatment, physicians might consider surgery as a means of assuring perhaps more rapid fracture union. However, we urge caution in utilizing only radiographic images as a means of guiding treatment in the presence of a partially united fracture. Clinical fracture tenderness or lack thereof may also play a role in deciding ongoing treatment. The influence of a partial CT scan union on clinical fracture tenderness or lack thereof (and vice versa) has not been studied to the best of our knowledge. Therefore, our thought process outlined above may very well be considered speculative. That being said, all the fractures included in this study went on to uneventful union, a fact that may add some credibility to our speculation.

Diagnosis of partial union may not be reliable enough for use in research, as suggested by contemporary data. Future research might further test reliability of this imaging modality. The accuracy of diagnosis of partial union might not be possible to study due to the lack of a reference standard as to what constitutes union as well as the location of union. An alternative approach would be to consider serial CT scans done 12 weeks apart, and analyzed by the same set of independent observers, which would allow quantification of ongoing union, as applicable in clinical care settings especially when combined with a consistently applied clinical exam by the same set of observers. This approach may very well allow us to develop guidelines as to when a scaphoid fracture can truly be considered to be clinically and radiologically united.

## REFERENCES

1. Dias JJ. Definition of union after acute fracture and surgery for fracture nonunion of the scaphoid. J Hand Surg Br. 2001, 26: 321-5.
2. Singh HP, Forward D, Davis TR, Dawson JS, Oni JA, Downing ND. Partial union of acute scaphoid fractures. J Hand Surg Br. 2005, 30: 440-5.
3. Grewal R, Suh N, Macdermid JC. Use of computed tomography to predict union and time to union in acute scaphoid fractures treated nonoperatively. J Hand Surg Am. 2013, 38: 872-7.
4. Siegel S CJ. Nonparametric Statistics for the Behavioral Sciences. 2nd Edn. New York, McGraw-Hill, 1988.
5. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics. 1977, 33: 159-74.
6. Mellema JJ, Mallee WH, Guitton TG, van Dijk CN, Ring D, Doornberg JN; Science of Variation Group & Traumaplatform Study Collaborative. Online Studies on Variation in Orthopedic Surgery: Computed Tomography in MPEG4 Versus DICOM Format. J Digit Imaging. 2017, Jan 24.
7. Desai VV, Davis TR, Barton NJ. The prognostic value and reproducibility of the radiological features of the fractured scaphoid. J Hand Surg Br. 1999, 24: 586-90.
8. Hannemann PF, Brouwers L, van der Zee D, Stadler A, Gottgens KW, Weijers R, Poeze M, Brink PR. Multiplanar reconstruction computed tomography for diagnosis of scaphoid waist fracture union: a prospective cohort analysis of accuracy and precision. Skeletal Radiol. 2013, 42: 1377-82.
9. Buijze GA, Wijffels MM, Guitton TG, Grewal R, van Dijk CN, Ring D; Science of Variation Group. Interobserver reliability of computed tomography to diagnose scaphoid waist fracture union. J Hand Surg Am. 2012, 37: 250-4.


BOSCHPOORT
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Fort Willemweg
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# Chapter 7

## Plain radiographs are reliable in distinction of nonunions from acute fractures of the scaphoid waist without computed tomography

Journal of Hand Surgery European Volume, 2018
**Drijkoningen T**, Guitton TG, Ring D

Dear Sir,
After a fall, a patient with an established scaphoid nonunion with or without associated arthritis may relate the problem to the recent event. These misconceptions might bias clinicians to misinterpret nonunions as acute fractures, with the potential for undertreatment (e.g. percutaneous screw fixation when debridement and bone grafting of the nonunion is needed). Computed tomography (CT) might help distinguish acute fractures from nonunions. In a study of 20 CT scans of healing scaphoid fracture and 10 confirmed nonunions the interobserver reliability of diagnosing scaphoid union was good (kappa of 0.66), but the negative predictive value was only 0.41, suggesting that CT is better for ruling in than ruling out union. (Buijze and Wijffels et al., 2012) The hypothesis of this study is that there is no agreement between observers on whether a scaphoid waist fracture is a nonunion or an acute fracture viewing radiographs alone compared to radiographs and CT-scans.
After approval of our institutional review board, members of the Science of Variation Group with an interest in hand or fracture surgery, were invited to participate in this study. Among the 161 surgeons that felt the study was appropriate for their expertise and interests, 157 completed the questionnaire. Radiographs and CT scans of patients with scaphoid waist fractures made within 30 days (acute fractures) or after 6 months (nonunions) of trauma were obtained from using billing codes via a research database. Inclusion criteria were: patients aged 18 years or older with a fracture of the scaphoid waist who had a radiograph and CT scan within 2 weeks of each other. Radiographs included a posteroanterior (PA) view, PA view with ulnar deviation of the wrist, and a lateral view. All scaphoid CT scans had a slice thickness of 1.25 mm or less. Separate movies showed a full series of CT scan images in the coronal plane and sagittal plane. Images were 0.625mm thickness, shown in bone windows. Radiographs were presented as static images on a web page: posteroanterior, lateral, and scaphoid views. Oblique views were not used because they were not always available. Participants were randomized 1:1 to view either radiographs alone or radiographs and videos of CT scans of 20 patients; 10 patients with acute scaphoid fractures and 10 patients having a nonunion. CT scans were obtained in the routine management of fractures and nonunions based on surgeon practice style. Observers were asked to diagnose if the fracture was acute or nonunited and to indicate the confidence in their answer. The vast majority of the 157 participants were men (n = 147). Forty percent specialized in hand and wrist surgery (n= 63) and 34 % in traumatology (n = 53)(Table 1).
There was substantial agreement on the age of the scaphoid fracture among observers that viewed radiographs alone ($\kappa = 0.73$) and observers that viewed radiographs and CT scans ($\kappa = 0.80$). Raters in the United States and Europe (compared to other parts of the world) had substantial agreement with radiographs alone and nearly perfect agreement when they also had a CT scan. Raters with 0-5 years in practice had substantial agreement. Raters who were more than 5 years in practice had an almost perfect agreement (table

2). The mean confidence of the observers viewing radiograph alone was 7.2 compared to 7.6 among observers that viewed radiographs and CT scans (p=0.21).

The limitations of our study include: data of tertiairy hospitals, spectrum bias (more nonunions than would be likely in a typical clinical scenario), and the very small possibility it had some of the fractures treated as acute were actually nonunions. Also presentation of the cases was standardized and observers were not able to adjust and manipulate images as would be the case in daily practice.

We found that distinction of nonunions from acute fractures of the scaphoid is reliable without a CT scan. Since in practice we have seen misdiagnosis of nonunions as acute fractures, the issue might be anchoring bias or other heuristics that can affect interpretation of diagnostic tests. We advise surgeons to be mindful of a small possibility that a seemingly new fracture is not acute.

Table 1: Characteristics of observers

| | n (%) |
|---|---|
| **Gender** | |
| Male | 147 (93.6) |
| Female | 10 (6.4) |
| **Location of practice** | |
| US/Canada | 81 (51.6) |
| Europe | 55 (35) |
| Asia | 5 (3.2) |
| Australia | 3 (2) |
| Other | 13 (8.2) |
| **Years in practice** | |
| 0 to 5 | 49 (31.2) |
| 6 to 10 | 39 (24.8) |
| 11 to 20 | 46 (29.3) |
| 21 to 30 | 23 (14.7) |
| **Supervising trainees** | |
| Yes | 135 (86) |
| No | 22 (14) |
| **Specialization** | |
| Hand-wrist | 63 (40.1) |
| Traumatolgy | 53 (33.7) |
| Shoulder/elbow | 26 (16.5) |
| General orthopedics | 7 (4.5) |
| Other | 8 (5.1) |

Table 2: Inter-observer agreement

| | Radiograph | | Radiograph and CT | |
|---|---|---|---|---|
| | Kappa | Agreement | Kappa | Agreement |
| **Overall** | 0.73 | substantial | 0.8 | substantial |
| | | | | |
| **Area** | | | | |
| United States | 0.77 | substantial | 0.82 | almost perfect |
| Europe | 0.7 | substantial | 0.82 | almost perfect |
| Other | 0.72 | substantial | 0.7 | substantial |
| | | | | |
| **Years in independent practice** | | | | |
| 0-5 | 0.75 | substantial | 0.73 | substantial |
| More than 5 years | 0.74 | substantial | 0.83 | almost perfect |

## REFERENCES


1. Buijze GA, Wijffels MM, Guitton TG, Grewal R, van Dijk CN, Ring D; Science of Variation Group. Interobserver reliability of computed tomography to diagnose scaphoid waist fracture union. J Hand Surg Am. 2012 Feb;37(2):250-4. doi: 10.1016/j.jhsa.2011.10.051
2. Desai VV, Davis TR, Barton NJ. The prognostic value and reproducibility of the radiological features of the fractured scaphoid. J Hand Surg Br. 1999 Oct;24(5):586-90
3. Herbert T J, Fisher W E. Management of the fractured scaphoid using a new bone screw. J Bone Joint Surg Br. 1984;66(1):114–123
4. Grewal R, Suh N, MacDermid JC. The Missed Scaphoid Fracture-Outcomes of Delayed Cast Treatment. J Wrist Surg. 2015 Nov;4(4):278-83. doi: 10.1055/s-0035-1564983

# PART IV

## FUTURE DIAGNOSTICS


Best
Strandpark Aquabest
Wilhelminadorp
Batadorp
Son
Keske
Houtens
Blixembosch
BOKT
Nederwet
WOENSEL-NOORD
Aanschot
WINKELCENTRUM
Boord
Eindhoven Airport
Technische Universiteit Eindhoven
STRIJP
N270
TONGELRE
STRIJP-S
Meerhoven
Eindhoven
Heistraat
HURK
Dommel
Boutenslaan
Piuslaan
GENNEP
Veldhoven
GESTEL
Veldhoven Dorp
Leenderheide
Aalst
Waalre
Achtereind
Heikant
N69
N620
A2
A50
A58
A67

# Chapter 8

## Inter-observer agreement between 2-dimensional versus 3-dimensional I-Space model in the diagnosis of occult scaphoid fractures

Archives of Bone and Joint Surgery, 2016
**Drijkoningen T**, Knotter R, Coerkamp EG, Koning AH, Rhemrev SJ, Beeres FJ

# Abstract

**Purpose:** The I-Space is a radiological imaging system in which Computed Tomography (CT)-scans can be evaluated as a three dimensional hologram. The aim of this study is to analyze the value of virtual reality (I-Space) in diagnosing acute occult scaphoid fractures.

**Methods and materials:** A convenient cohort of 24 patients with a CT-scan from prior studies, without a scaphoid fracture on radiograph, yet high clinical suspicion of a fracture, were included in this study. CT-scans were evaluated in the I-Space by 7 observers of which 3 observers assessed the scans in the I-Space twice. The observers in this study assessed in the I-Space whether the patient had a scaphoid fracture. The kappa value was calculated for inter- and intra-observer agreement.

**Results:** The Kappa value varied from 0.11 to 0.33 for the first assessment. For the three observers who assessed the CT-scans twice; observer 1 improved from a kappa of 0.33 to 0.50 (95% CI 0.26-0.74, $P$=0.01), observer 2 from 0.17 to 0.78 (95% CI 0.36-1.0, $P$<0.001), and observer 3 from 0.11 to 0.24 (95% CI 0.0-0.77, $P$=0.24).

**Conclusion:** Following our findings the I-Space has a fast learning curve and has a potential place in the diagnostic modalities for suspected scaphoid fractures.

## INTRODUCTION

Hand trauma frequently occurs, especially in young male adults (1,2). When diagnosing scaphoid fractures, knowledge is needed of the anatomy and common fracture patterns of the bone. Specialized radiographic views or additional imaging is needed (3). To date no consensus regarding different diagnostic modalities has shown to be the gold standard (2).
An example of a diagnostic modality is the I-Space; a CAVE-like virtual reality system (Fig. 1). A "hologram" of a 3D modality dataset is visualized as a floating image in front of the viewers. The viewers wear a pair of glasses with polarizing lenses that allow the bony structures to be seen as free-floating objects in three dimensions. An advantage is that a virtual pointer can be used to interact with this "hologram". This makes it possible to 'slice' through the hologram and to perform all kinds of measurements. In other fields very promising results are shown using this method (4-10).
In this pilot study CT-scans of patients suspected of an occult scaphoid fracture, were analyzed using the I-Space. The aim of this study is to analyze the inter-observer agreement of the current most used modality (CT-scan (2D view)) compared to virtual reality (3D view) in diagnosing occult scaphoid fractures.

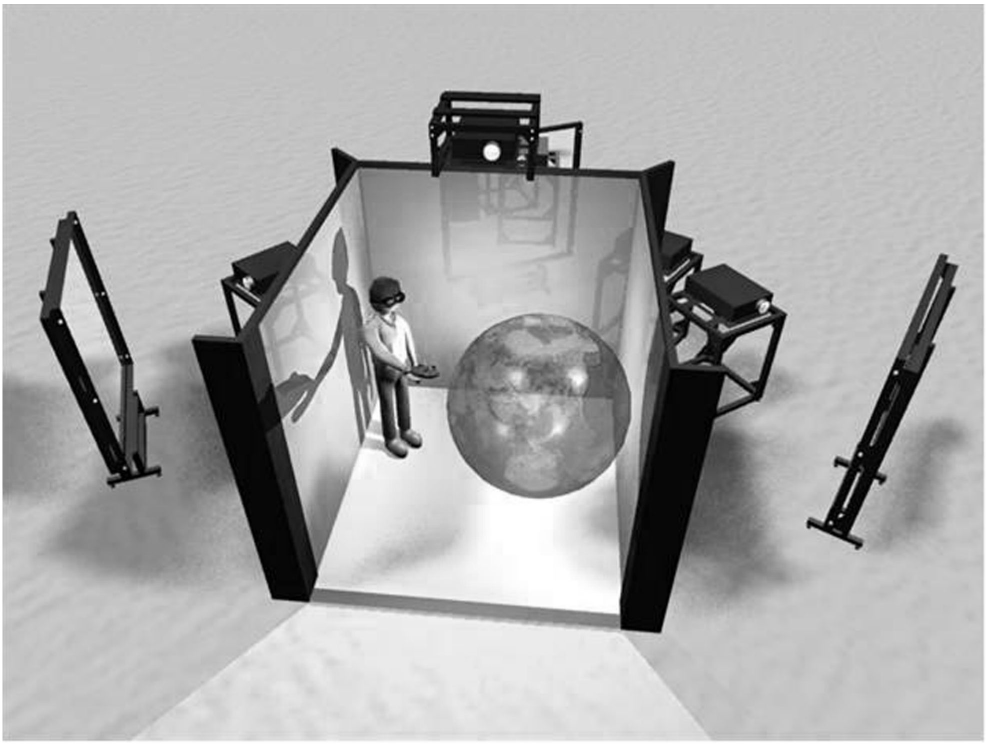

**Figure 1.** I-space concept

# METHODS

## Design

This study used data from a prior study, a convenient sample comprised of 24 of 149 patients, with a high clinical suspicion of a scaphoid fracture but no fracture on radiograph. All patients had undergone a CT-scan, at the Emergency Department of one hospital. In all patients the CT scan was performed within 24 hours after presentation according to a standardized protocol (1). The 2D CT-scans were initially assessed for fractures of the scaphoid by 2 physicians and 2 residents. CT-scans with slice thickness >1.5 mm will not produce a reliable 3D reproduction in the I-Space, therefore hundred twenty patients were excluded because CT-scan images had a slice thickness of more than 1.5 mm. Five patients were excluded as they had multiple fractures in the carpal bones. In this study the images were assessed by seven observers in the I-space (a CAVE-like virtual reality system) after conversion.

To measure inter-observer reliability seven observers viewed the blinded CT scans in the I-Space and were asked to diagnose the presence of a scaphoid fracture (Fig. 2). Three of the seven observers also assessed the 2D CT-scans 5 years before this study. Three of the seven observers assessed the CT-scans twice in the I-Space. Scans were randomized the second time and time between the sessions was at least 3 weeks.

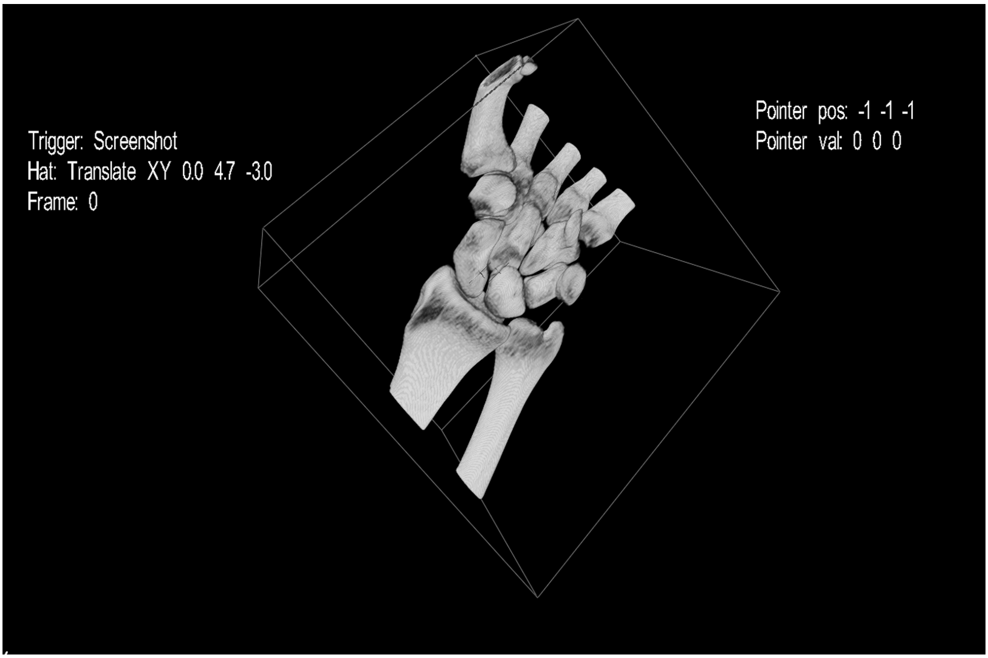


**Figure 2.** Scaphoid in the I-space

Patients gave their written consent and permission in the original studies to use their data for future studies and institutional approval for the use of study data was granted by the Medical Review Board of our institute.

## Radiology

The Computed radiography system; General Electric Lightspeed Qx/GT 64-slice Scanner Pewaukee, WI was used. The patient was lying on the scanner couch with the involved hand extended forward palm down. The wrist was laying in neutral flexion and neutral radial ulnar deviation (1). CT was performed by standard protocol (1). Some patients had to be scanned with their cast on for clinical reasons. The CT-images were transferred to the I-Space (Barco NV, Kortrijk, Belgium), at the department of Bioinformatics, Erasmus MC (Rotterdam, Netherlands).

The I-Space is a four-walled CAVE TM-like virtual reality system. Eight projectors create 3D images that can be seen using a set of polarizing glasses. The V-Scope volume rendering application creates an interactive "hologram" of the CT-dataset and is used to perform measurements. The dataset can be manipulated (e.g., rotated, resized) interactively using a wireless joystick projecting a virtual pointer. The user can turn on a clipping plane that is attached to the virtual pointer, thereby allowing intuitive placement. In addition the dataset can be rotated while manipulating the clipping plane, making it very simple to investigate suspected areas from different angles. The depth perception offered by the I-Space enhances the visualization of fractures. Finally the transparency and contrast of bone as well as soft tissue can interactively be changed, which may increase the visibility of fractures.

## Statistical analysis

A consensus of 2 physicians and 2 training physicians for the 2D assessment of the CT-scan was used as the gold standard in this study (1). The observer demographics and patient characteristics were described with frequencies and percentages for categorical variables and with mean ± standard deviation and range for continuous variables. The kappa value was calculated for inter- and intra-observer agreement, also it was determined whether a second assessment in the I-Space correlated with improvement in intra-observer agreement. Kappa is a quantitative measure of agreement among observers and takes into account that observers will sometimes choose the same answer to a question by chance (11). A perfect agreement among observers would be reflected as a kappa of 1, whereas agreement totally based on chance would equate to a kappa of 0. Interpretation of kappa often is done by a classification by Landis and Koch (12) in which a kappa between 0.01 and 0.20 is considered to reflect slight agreement, a value between 0.21 and 0.40 as fair agreement, between 0.41 to 0.60 as moderate agreement, 0.61 and 0.80 as substantial agreement, and greater than 0.81 as almost perfect agreement.

## Baseline caracteristics

Twenty-four patients were included from two prior studies. No Patients had signs of a fracture on conventional X-ray. A total of 3 (12.5%) patients were diagnosed with definite fractures of the scaphoid on the CT-scan. The mean age for all patients was 36 years (range 18-60) with 14 (58.3%) males and 10 (41.7%) females. (Table 1)

Table 1: Observer Demographics

| | obs 1 | obs 2 | obs 3 | obs 4 | obs 5 | obs 6 | obs 7 |
|---|---|---|---|---|---|---|---|
| **Male/Female** | male | male | female | male | male | male | male |
| **Certified Physician/ Resident** | physician | resident | resident | resident | resident | physician | resident |
| **Years in practice** | 10 to 15 | 5 to 10 | 0 to 5 | 0 to 5 | 5 to 10 | 20 to 25 | 0 to 5 |
| **Specialty** | surgery | surgery | radiology | surgery | surgery | radiology | surgery |

# RESULTS

A total of seven observers assessed the CT-images of all patients in the I-Space. Two of the observers were a radiologist and a resident radiology, one was a surgeon and four were surgery residents. (Table 2) There was a variable range of years in practice. The Kappa value for the agreement for each observer assessing the images in the I-space versus the result of the CT-scan, conducted from assessment of 4 observers in the previous study was calculated. The lowest Kappa value measured was 0.11, the highest value was 0.33 for the first assessment. (Table 3)

Table 2: Patient characteristics (n=24)

| Characteristic | Number |
|---|---|
| **Mean age (range)** | 36 (18-60) |
| **Male sex (%)** | 14 (58.3 %) |
| | |
| **Positive scinigraphy (%)** | 6 (25 %) |
| **Positive CT-scan (%)** | 3 (12.5 %) |

Table 3: Level of agreement I-space vs CT-scan

| | Kappa (1st assessment) (95% CI, P-value) | Kappa 2nd assessment) (95% CI, P-value) |
|---|---|---|
| **Observer 1** | 0,33 (0,0-0,78, P=0.08) | 0,50 (0,26-0,74, P=0.01) |
| **Observer 2** | 0,17 (0,0-0,65, P=0,41) | 0,78 (0,36-1,0, P<0.001) |
| **Observer 3** | 0,11 (0,0-0,55, P=0,57) | 0,24 (0,0-0,77, P=0,24) |
| **Observer 4** | 0,11 (0,0-0,40, P=0,44) | n.a. |
| **Observer 5** | 0,17 (0,0-0,65, P=0,41) | n.a. |
| **Observer 6** | 0,33 (0,0-0,77, P=0,08) | n.a. |
| **Observer 7** | 0,33 (0,0-0,91, P=0,09 | n.a. |

The three observers that reviewed the images for a second time in the I-Space showed greater level of agreement between 2D CT and 3D I-Space models: the kappa value for observer 1 improved from 0.33 to 0.50 (95% CI 0.26-0.74, $P$=0.01), observer 2 from 0.17 to 0.78 (95% CI 0.36-1.0, $P$<0.001), and observer 3 from 0.11 to 0.24 (95% CI 0.0-0.77, $P$=0.24). (Table 4)

The Fleiss Kappa for inter-observer agreement for all observers in the I-space was 0.20 (95% CI 0.07-0.39, $P$=0.00). When analyzing the subset of observers that performed a second assessment in the I-space it is shown that inter-observer agreement improved from 0.01 (95% CI 0.0-0.36, $P$=0.252) for the first assessment to 0.37 (95% CI 0.12-0.63, $P$=0.001) for the second assessment. (Table 5)

Table 4: Level of agreement two assessments I-space

| | Kappa (95% CI, P-value) |
|---|---|
| **Observer 1** | 0,25 (0,0-0,69, P=0,21) |
| **Observer 2** | 0,25 (0,0-0,76, P=0,19) |
| **Observer 3** | 0,41 (0,0-0,87, P=0,04) |

Table 5: Levels of agreement I-space

| | Fleiss Kappa (95% CI, P-value) |
|---|---|
| **All observers** | 0,20 (0,07-0,39, P=0.000) |
| **3 observers, 1st assessment** | 0,01 (0,0-0,36, P=0,252) |
| **3 observers, 2nd assessment** | 0,37 (0,12-0,63, P=0,001) |

## DISCUSSION

The I-Space is a fairly new 3D-display modality, which is rarely used in clinical settings. This pilot study using this 3D-display modality was performed, as there is no golden standard in diagnosing scaphoid fractures. (2) Results of this study suggest that the I-space is a modality with a fast learning curve and a potential clinical usefulness to assess occult fractures.

Previous studies point out that CT-scans are comparable in diagnosing scaphoid fractures to MRI (2) and that in both modalities fractures of the scaphoid can be missed. Imaging modalities such as the I-Space were until now mostly used in research setting and for soft tissue studies (4-7,9,10). One prior study was published using the I-Space focusing on postoperative anterior cruciate ligament reconstruction. They found the best inter-observer agreement when using the I-Space compared to normal CT-views (3).

The first limitation is the fact that there is no gold standard in diagnosing scaphoid fractures. In this study we compared the results in the I-Space with the results from the CT-scans. The CT-scans were performed for use in a prior study, consequently 125 patients had to be excluded due to incomplete saving of all CT slices or the saved slices were too thick. This results in loss of power, however for this pilot study the power remains adequate. No systematic bias was introduced by excluding these patients, for quality of the scans was the selection criterium. The quality of some of the images was low as a number of scans were performed while the patients arm was in a plaster cast. As this was the same for the 2D viewed CT-scans we assume that this should not make a difference. Making CT-scans without a cast is recommended in general, as less radiation is needed.

*How can the present results be explained?* None of the observers had previously assessed images in the I-Space. As a result, the level of agreement for the first assessment in the I-Space with conventional CT-images is poor (kappa range 0.11 – 0.33), the intra-observer level of agreement for the I-space was poor as well (Fleiss kappa 0.20). All patients included in this study had a clinical suspicion of an occult fracture not visible on radiographs, making images difficult to assess in any modality. Furthermore, previous literature shows variable intra- and inter-observer reliability for CT-scan as the primary imaging modality in optimal conditions as well (13). Amongst the 3 observers who viewed the images twice in the I-Space the intra-observer agreement rose significantly for the second assessment. This trend was also shown in a comparison of the inter-observer reliability in these 3 observers (0.01 to 0.37). These results suggest that the I-space is an easy modality to learn which could be good for teaching purposes. At this point it is difficult to predict the exact diagnostic value as this is a fairly new modality for fracture diagnosis.

*What are the clinical implications?* Viewing CT-images in the I-Space 3D-display might be useful in pre-operative planning and teaching settings as the images help picturing a complete 3D view. Anatomical details can be realistically pictured on a great scale in the I-Space, resulting in a very illustrative overall picture for training physicians. For the I-Space method a separate room with projectors is needed, consequently it might not be feasible in every hospital setting. Although in teaching hospitals it could be of worthwhile investment. The system is user friendly and will not take much time getting used to. These advantages might make this a new progressive imaging device in clinical settings.

The aim of this study was to get pilot data on the diagnostic value of the I-Space in detecting occult scaphoid fractures. Following our findings the I-Space has a fast learning curve. We carefully recommend the use of the I-Space in pre-operative planning and for teaching purposes. Our recommendation is do more studies using the I-Space with a separate scanning-protocol and optimal image quality when searching for the diagnostic value in occult scaphoid fractures. Moreover would it be worthwhile to study the value in pre-operative planning and teaching for physicians.

## REFERENCES


1. Rhemrev SJ, de Zwart AD, Kingma LM, Meylaerts SA, Arndt JW, Schipper IB et al. Early computed tomography compared with bone scintigraphy in suspected scaphoid fractures. Clin Nucl Med. 2010 Dec; 35(12): 931-4
2. Mallee WH, Wang J, Poolman RW, Kloen P, Maas M, de Vet HC, et al. Computed tomography versus magnetic resonance imaging versus bone scintigraphy for clinically suspected scaphoid fractures in patients with negative plain radiographs. Cochrane Database Syst Rev. 2015 Jun 5;6: CD010023
3. Hannemann PF, Brouwers L, Dullaert K, van der Linden ES, Poeze M, Brink PR. Determining scaphoid waist fracture union by radiographic examination: an analysis of reliability and validity. Arch Orthop Trauma Surg. 2015 Feb;135(2):291-6. doi: 10.1007/s00402-014-2147-9. Epub 2015 Jan 3
4. Timmermans L, Deerenberg EB, van Dijk SM, Lamme B, Koning AH, Kleinrensink GJ. et al. Abdominal rectus muscle atrophy and midline shift after colostomy creation. Surgery. 2014 Apr;155(4):696-701
5. Meuffels DE, Potters JW, Koning AH, Brown CH Jr, Verhaar JA, Reijman M.
Visualization of postoperative anterior cruciate ligament reconstruction bone tunnels: reliability of standard radiographs, CT scans, and 3D virtual reality images.
Acta Orthop. 2011 Dec;82(6):699-703
6. van Adrichem LN, van Vlimmeren LA, Cadanová D, Helders PJ, Engelbert RH, van Neck HJ et al. Validation of a simple method for measuring cranial deformities (plagiocephalometry). J Craniofac Surg. 2008 Jan; 19(1): 15-21
7. Baken L, van Gruting IM, Steegers EA, van der Spek PJ, Exalto N, Koning AH. Design and validation of a 3D virtual reality desktop system for sonographic length and volume measurements in early pregnancy evaluation. J Clin Ultrasound. 2015 Mar; 43(3):164-70
8. Baken L, Rousian M, Koning AH, Bonsel GJ, Eggink AJ, Cornette JM et al. First-Trimester Detection of Surface Abnormalities: A Comparison of 2- and 3-Dimensional Ultrasound and 3-Dimensional Virtual Reality Ultrasound. Reprod Sci. 2014 Jan 18;21(8):993-999
9. Rifouna MS, Reus AD, Koning AH, van der Spek PJ, Exalto N, Steegers EA, et al. First trimester trophoblast and placental bed vascular volume measurements in IVF or IVF/ICSI pregnancies. Hum Reprod. 2014 Dec; 29(12):2644-9
10. Baken L, van Heesch PN, Wildschut HI, Koning AH, van der Spek PJ, Steegers EA, et al. First-trimester crown-rump length and embryonic volume of aneuploid fetuses measured in virtual reality. Ultrasound Obstet Gynecol. 2013 May;41(5):521-5
11. Viera AJ, Garrett JM. Understanding interobserver agreement: the kappa statistic. Fam Med. 2005;37:360–363
12. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics. 1977;33:159–174
13. Adey L, Souer JS, Lozano-Calderon S, Palmer W, Lee S, Ring D. Computed tomography of suspected scaphoid fractures. J Hand Surg Am. 2007 Jan;32(1):61-66

# PART V

## GENERAL DISCUSSION


N516
s118
Landsmeer
Nieuwe Gouw
Het Schouw
Molenwijk
De Zuid
N247
A10
TUINDORP
OOSTZAAN
s117
't Nopeind
Zunderdorp
Buiksloot
NDSM-werf
s116
A5
s101
s118
AMSTERDAM-NOORD
S102
HOUTHAVENS
Eye Film Museum
Westerpark
s103
s116
A10
Anne Frank Huis
NEMO Science Museum
A10
s100
ZEEBURG
s114
Amsterdam
Brewery
Heineken Experience
A10
Vondelpark
DE PIJP
WATERGRAAFSMEER
s110
s108
s112
A1
Amstel Business Park
Diemen
AMSTERDAM-ZUID
s113
Duivendrecht
Buitenveldert
Amstelpark
A2
Stadium
Johan Cruijff ArenA
Bijlmermeer
Amstelveen
Amstel
s108
STADSHART
N522

# Chapter 9

## Discussion & Summary

## General Discussion

Scaphoid fractures are the most common hand fractures diagnosed in the emergency room in hospitals around the world.[1] In the past few decades, much endeavor has been done to identify the acute scaphoid fracture patterns that are prone to nonunion for purposes of surgical decision making. However, a reliable classification and a gold standard for imaging and reproducible ways to interpret existing imaging methods still have to be found. This thesis aimed to gain knowledge and improve classification and imaging in scaphoid fractures.

CLASSIFYING SCAPHOID FRACTURES

In **Chapter 1** a literature overview showed that over a dozen classification systems have been proposed and were mainly based on fracture location or displacement. Considering the number of citations, the Herbert classification was most popular, followed by the Russe and Mayo classification. Based on original reports describing fracture location,[2-4] waist fractures occur most often with percentages ranging from 66 to 82%. Considering fracture plane orientation[3,5,6] transverse fractures have the highest incidence ranging from 36% to 60%, followed by horizontal oblique fractures ranging from 30% to 47%. Considering fracture stability,[2,7] most fractures are described as stable (53% and 71%).

In **Chapter 2** our 3D fracture mapping study showed that all scaphoid fractures in the proximal and middle third of the bone were similar horizontal oblique type fractures with a single common fracture area in the middle third. None of the most distal fractures go through - but only directly proximal to - the tubercle suggesting that these would be best classified as distal waist fractures. To investigate whether these notable findings were consistent with larger series a secondary analysis of a similar previously published series of 124 scaphoid models was performed including 13 distal third fractures.[8] This type of distal third fracture is more commonly referred to as a scaphoid tubercle fracture.[9] Combining these data we suggested a new simplified classification for scaphoid fractures; 1) proximal pole fractures (proximal to the distal scapholunate (SL) interval), (2) a range of waist fractures (involving the scaphocapitate (SC) interval), and (3) distal tubercle fractures (involving the STT interval). In this study we had a highly selective group of patients with a CT-scan with a slice thickness 1.25 mm or smaller. This introduced sampling bias as the subset of patients may not be representative of the average patient with a scaphoid fracture. In particular, these fractures were likely either difficult to diagnose on radiographs or they were evaluated for the likelihood of displacement. Our impression is that these fractures are most representative of the subset of fractures that are more than a small distal tubercle fracture.

Our proposed simplified classification can also improve comparison of studies on scaphoid fractures, as it simple and more reproducible, which we have shown in **Chapter 3.** This chapter shows that the simplified scaphoid fracture classification was easily reproducible in a large series of scaphoid fractures and fractures that do not fit this classification are rare. An additional inter-observer study compared the simplified classification with the Herbert classification and showed fair agreement for both classifications but significantly less doubt when classifying scaphoid fractures using the simplified classification. In this study we had a relatively low number of proximal pole (n = 30) and distal tubercle fractures (n = 39) hindered multivariable statistical analysis. A larger sample with more proximal pole and distal tubercle fractures might have resulted in more statistical power to detect subtle but relevant differences between different fracture types.

Classifying scaphoid fractures allows for a more targeted offering of treatment. As none of the known classifications are able to predict the prognosis, especially nonunion of the scaphoid, future research should lead to a reliable classification. Graham *et al* looked at 60 patients with acute fractures with both radiographs and CT-scans and classified them according to Russe, Herbert, Mayo and their pragmatic 'long axis measurement'.[10] On plain PA-radiographs or CT-image with the best long-axis view, the proximal point of the scaphoid and distal point were marked and connected with a line. A perpendicular line was drawn at the proximal end and distance to the fracture line was measured. Using the long-axis measurement they found a substantial inter and intra-observer reliability.

Further studies might focus on finding a reliable way to identify substantial interfragmentary motion when displacement is ruled out. Secondly look further into fracture instability in relation to the location relative to the dorsal apex as shown in nonunions. Thirdly a large multi-institutional database study might help to incorporate more proximal pole and tubercle fractures necessary to study the epidemiology of these fractures.

## PHYSICIAN INTERPRETATION OF DIAGNOSTICS

As the patients' treatment is mostly based on imaging, it is valuable to interpret diagnostic images similarly. In **Chapter 4** the interobserver variability in diagnosis of scaphoid proximal pole fractures showed no difference in agreement on diagnosis of scaphoid fracture location with the use of either radiographs alone or when radiographs were accompanied by a CT-scan. The reliability was high for both. This study suggests that computed tomography does not meaningfully improve the reliability of diagnosis of fracture location (which is almost perfect) or displacement (which is fair) in the scaphoid. However, most observers worked in an academic setting (90% supervises trainees) and their values, training, and practice might differ from the larger community of surgeons.

Healing tendency of scaphoid fractures is often assessed using CT-scans. We studied if CT is really necessary as it is increasingly used to diagnose union, and estimate the percentage bony bridging of the fracture gap. In **Chapter 5** we concluded there is limited reliability of diagnosis of partial union of a scaphoid waist fracture on computed tomography and that this should be taken into account in both patient care and research.

Although we do think that quantifying degree of bony bridging may have an impact on treatment.

Interpreting images and diagnose the age of a scaphoid fracture is what we studied in **Chapter 6**. We found that distinction of nonunions from acute fractures of the scaphoid is reliable with just a radiograph and without a CT scan. Since in practice we have seen misdiagnosis of nonunions as acute fractures, the issue might be anchoring bias or other heuristics that can affect interpretation of diagnostic tests. Moreover misconceptions might bias clinicians to misinterpret nonunions as acute fractures, with the potential for undertreatment (e.g. percutaneous screw fixation when debridement and bone grafting of the nonunion is needed).

For all 3 studies images were presented in a standardized fashion, which did not allow observers to adjust and manipulate images as would be the case in their daily practice. However, a study found the format of imaging visualization, has limited influence on interpretation.[11]

Current best evidence shows that there is no consensus not only in classifying scaphoid fractures but also in interpreting diagnostic imaging. This suggests that there is a wide variation in treatment of acute scaphoid fracture. Fracture union over 50% of a scaphoid fracture on imaging will give direction in fracture treatment. However, Brekke *et al* studied the biomechnical strength of partial union in 41 cadaver scaphoids and found no significant variance in average maximum load between an 100% intact scaphoid and a non-displaced waist fracture with 25% bony bridging.[12] As diagnosis of partial union is limited but a minimum of 25% bony bridging is sufficient in terms of loadability, slight differences in diagnosis of bridging might not be a clinical issue.

Future studies might look into wrist-motion using fluoroscopy and dynamic three-dimensional CT may be useful to find predictors for interfragmentary motion (i.e. true instability) in relation to surgical or arthroscopic findings and clinical outcome. Also studying the impact of training and clear definitions of specific fracture types and displacement. It may be that proximal pole fractures are sufficiently distinct from proximal waist fractures that sophisticated imaging is unnecessary. Thirdly further test reliability of CT-scans although the accuracy of diagnosis of partial union might not be possible to study due to the lack of a reference standard as to what constitutes union as well as the location of fracture union. And finally develop guidelines as to when a scaphoid fracture can truly be considered clinically and radiologically united will be valuable for patient care.



## FUTURE DIAGNOSTICS

In **Chapter 7** the I-Space was used to assess the value in diagnosing occult scaphoid fractures.[13-20] Anatomic details of fractures can be realistically pictured on a great scale as a hologram in the I-Space, resulting in a very illustrative overall picture for physicians in training. In teaching hospitals it could be a worthwhile investment in pre-operative planning and for teaching purposes. Although we found that for diagnosing occult fractures this might not be more valuable than viewing a CT-scan in two dimensions. Studying a new imaging technique is challenging as there is no gold standard in diagnosing scaphoid fractures. The use of the I-Space with a detailed scanning-protocol in further studies could optimize image quality when searching for the diagnostic value in occult scaphoid fractures and might make future studies more valuable. As advanced imaging in some cases is not readily available also ultrasounds might be able to diagnose occult scaphoid fractures radiographically with a fairly high degree of accuracy.[21]

## References


1. Hove LM. Epidemiology of scaphoid fractures in Bergen, Norway. Scand J Plast Reconstr Surg Hand Surg. 1999;33:423–426.
2. Cooney WP, Dobyns JH, Linscheid RL. Fractures of the scaphoid: a rational approach to management. Clin Orthop Relat Res. 1980(149):90-97
3. Bohler L, Trojan E, Jahna H. [Treatment of 734 cases of fresh fracture of the scaphoid bone of the hand]. Wiederherstellungschir Traumatol. 1954;II:86-111
4. Schernberg F, Elzein F, Gerard Y. [Anatomo-radiological study of fractures of the carpal scaphoid bone. Problems of abnormal callus]. Rev Chir Orthop Reparatrice Appar Mot. 984;70 Suppl 2:55-63
5. Russe O. Fracture of the carpal navicular. Diagnosis, non-operative treatment, and operative treatment. J Bone Joint Surg Am. 1960;42-A:759-768
6. Compson JP. The anatomy 257 of acute scaphoid fractures: a three-dimensional analysis of patterns. J Bone Joint Surg Br. 1998;80(2):218-224
7. Weber ER. Biomechanical implications of scaphoid waist fractures. Clin Orthop Relat Res. 1980(149):83-89
8. Luria S, Schwarcz Y, Wollstein R, Emelife P, Zinger G, Peleg E. 3-dimensional analysis of scaphoid fracture angle morphology. J Hand Surg Am. 2015 Mar;40(3):508-514. doi: 10.1016/j.jhsa.2014.11.008. Epub 2015 Jan 9
9. Kraus R, Böhringer G, Meyer C, Stahl JP, Schnettler R. [Fractures of the scaphoid tubercle]. Handchir Mikrochir Plast Chir. 2005 Apr;37(2):79-84. German.
10. Dean BJF, Riley ND, McCulloch ER, Lane JCE, Touzell AB, Graham AJ. A new acute scaphoid fracture assessment method: a reliability study of the 'long axis' measurement. BMC Musculoskelet Disord. 2018 Aug 29;19(1):310. doi: 10.1186/s12891-018-2236-y.
11. Mellema JJ, Mallee WH, Guitton TG, van Dijk CN, Ring D, Doornberg JN; Science of Variation Group & Traumaplatform Study Collaborative. Online Studies on Variation in Orthopedic Surgery: Computed Tomography in MPEG4 Versus DICOM Format. J Digit Imaging. 2017, Jan 24.
12. Brekke AC, Snoddy MC, Lee DH, Richard MJ, Desai. Biomechanical Strength of Scaphoid Partial Unions. MJ.J Wrist Surg. 2018 Nov;7(5):399-403. doi: 10.1055/s-0038-1661362. Epub 2018 Jun 26.
13. Timmermans L, Deerenberg EB, van Dijk SM, Lamme B, Koning AH, Kleinrensink GJ. et al. Abdominal rectus muscle atrophy and midline shift after colostomy creation. Surgery. 2014 Apr;155(4):696-701
14. Meuffels DE, Potters JW, Koning AH, Brown CH Jr, Verhaar JA, Reijman M.
    Visualization of postoperative anterior cruciate ligament reconstruction bone tunnels: reliability of standard radiographs, CT scans, and 3D virtual reality images.
    Acta Orthop. 2011 Dec;82(6):699-703


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15. van Adrichem LN, van Vlimmeren LA, Cadanová D, Helders PJ, Engelbert RH, van Neck HJ et al. Validation of a simple method for measuring cranial deformities (plagiocephalometry). J Craniofac Surg. 2008 Jan; 19(1): 15-21
16. Baken L, van Gruting IM, Steegers EA, van der Spek PJ, Exalto N, Koning AH. Design and validation of a 3D virtual reality desktop system for sonographic length and volume measurements in early pregnancy evaluation. J Clin Ultrasound. 2015 Mar; 43(3):164-70
17. Baken L, Rousian M, Koning AH, Bonsel GJ, Eggink AJ, Cornette JM et al. First-Trimester Detection of Surface Abnormalities: A Comparison of 2- and 3-Dimensional Ultrasound and 3-Dimensional Virtual Reality Ultrasound. Reprod Sci. 2014 Jan 18;21(8):993-999
18. Rifouna MS, Reus AD, Koning AH, van der Spek PJ, Exalto N, Steegers EA, et al. First trimester trophoblast and placental bed vascular volume measurements in IVF or IVF/ICSI pregnancies. Hum Reprod. 2014 Dec; 29(12):2644-9
19. Baken L, van Heesch PN, Wildschut HI, Koning AH, van der Spek PJ, Steegers EA, et al. First-trimester crown-rump length and embryonic volume of aneuploid fetuses measured in virtual reality. Ultrasound Obstet Gynecol. 2013 May;41(5):521-5
20. Steinmann SP, Adams JE. Scaphoid fractures and nonunions: diagnosis and treatment. J Orthop Sci. 2006;11:424–431
21. Kwee RM, Kwee TC. Ultrasound for diagnosing radiographically occult scaphoid fracture. Skeletal Radiol. 2018 Sep;47(9):1205-1212. doi: 10.1007/s00256-018-2931-7. Epub 2018 Apr 4.

## Summary

Scaphoid fractures are among the most common wrist fractures of patients presenting to the emergency room. These fractures were first described in 1905 by Destot, a French pioneer in analyzing wrist problems followed by the discovery of radiography. Destot combined studying wrist anatomy, radiographic interpretations and clinical conditions which lead to a classification of various carpal injuries including a classification for scaphoid fractures. Shortly after, scaphoid fractures became notorious for their troublesome healing.

**Chapter 1** shows that over the last few decades several classification systems and imaging technologies have been proposed for scaphoid fractures. Improvement in diagnosis of fractures is much needed to predict healing and select optimal treatment ranging from cast immobilization to internal fixation. Currently, the Russe, Mayo, and Herbert systems are commonly used in clinical practice. These classifications are based on fracture planes, fracture location and stability, respectively. However, studies have shown that reliable prediction model of fracture union cannot be provided by these classification systems, and classification itself has poor reproducibility.

In **Chapter 2** scaphoid fractures were imaged using 3D imaging techniques. With the introduction of 3D imaging analyses and new techniques like fracture mapping, new insights of wrist kinematics and patterns in scaphoid fractures and deformity are proposed. This study shows that all scaphoid fractures in the proximal and middle third of the bone were similar horizontal oblique type fractures with a single common fracture area in the middle third of the bone. Using these data we suggested a new simplified classification for scaphoid fractures; 1) proximal pole fractures (proximal to the distal scapholunate (SL) interval), (2) a range of waist fractures (involving the scaphocapitate (SC) interval), and (3) distal tubercle fractures (involving the STT interval).

In **Chapter 3** the simplified scaphoid fracture classification was first taken in use in a database study and an inter-observer study. It shows to be easily reproducible in a large series and fractures that do not fit this classification are rare. The additional inter-observer study compared the simplified classification with the Herbert classification and showed fair agreement for both classifications but significantly less doubt by the observers when classifying scaphoid fractures using the simplified classification

In **Chapter 4** radiographs and CT-scans are used to diagnose proximal pole scaphoid fractures using an interobserver study. The variability in diagnosis of scaphoid proximal pole fractures showed no difference in agreement on diagnosis of scaphoid fracture location with the use of either radiographs alone or when radiographs were accompanied by a CT-scan. The reliability was high for both. This study suggests that computed tomography does not meaningfully improve the reliability of diagnosis of fracture location (which is almost perfect) or displacement (which is fair) in the scaphoid.

In **Chapter 5** we tested the agreement between observers on the extent of union of a scaphoid waist fracture on computed tomography. Observers were asked to 'eyeball' measure percentage of union. We found that there was a moderate agreement on the categorical degree of partial union of a scaphoid waist fracture on computed tomography. Agreement on the location of bony bridging was slight. We concluded there is limited reliability of diagnosis of partial union of a scaphoid waist fracture on computed tomography and that this should be taken into account in both patient care and research. Although we do think that quantifying degree of bony bridging may have an impact on treatment.

In **Chapter 6** we studied if physician can determine if a scaphoid fractures are acute or nonunited using radiographs and CT-scans. We looked into this as treatment for fresh and delayed fractures are different. The agreement was substantial in the age of the scaphoid fracture among observers that viewed radiographs alone and observers that viewed radiographs and CT scans. We found that distinction of nonunions from acute fractures of the scaphoid is reliable without a CT scan. Since in practice we have seen misdiagnosis of nonunions as acute fractures, the issue might be anchoring bias or other heuristics that can affect interpretation of diagnostic tests.

In **Chapter 7** new imaging modalities such as the I-Space, a virtual reality system, was until now mostly used in research setting and for soft tissue studies. The I-Space method uses a separate room with projectors to view the images as a hologram. We used the it to assess the value in diagnosing scaphoid fractures which are not diagnosed in the first visit. Results of this study suggest that the I-space is a modality with a fast learning curve and a potential clinical usefulness to assess occult fractures. Anatomic details can be realistically pictured on a great scale in the I-Space, resulting in a very illustrative overall picture for training physicians.

## Samenvatting

Scaphoïd fracturen behoren tot de meest voorkomende polsbreuken bij patiënten die de eerste hulp bezoeken. Deze breuken werden voor het eerst beschreven in 1905 door Destot, een Franse pionier in het analyseren van polsproblemen. Dit als gevolg van de ontdekking van de radiografie.. Destot combineerde de polsanatomie, radiografische interpretaties en klinische tekenen leidend tot een classificatie van verschillende carpale letsels inclusief een classificatie voor scafoïdfracturen. Korte tijd daarna werden scafoïd fracturen berucht vanwege hun lastige genezing.

In **Hoofdstuk 1** wordt aangetoond dat in de laatste decennia verschillende classificatiesystemen en beeldvormingstechnologieën zijn beschreven voor scafoïd fracturen en de diagnose daarvan om de genezing te begrijpen en een optimale behandeling te kiezen. Een behandeling kan gips zijn of een operatie met interne fixatie. Momenteel zijn de Russe, Mayo en Herbert-classificatie systemen het meest gebruikt in klinische praktijken. Deze classificaties zijn gebaseerd op respectievelijk breukvlakken, fractuurlocatie en stabiliteit. Studies hebben echter aangetoond dat deze classificatiesystemen geen betrouwbaar voorspellingsmodel voor deze fracturen kunnen bieden en dat de classificaties zelf niet goed reproduceerbaar zijn.

In **Hoofdstuk 2** worden scapoïd fracturen geanalyseerd met behulp van 3D-beeldvormingstechnieken. Met de introductie van 3D beeldvorming en nieuwe technieken zoals 'fracture mapping', worden nieuwe inzichten in pols-kinematica en patronen in scafoïd breuken gevonden. Deze studie toont aan dat alle scafoïd fracturen in het proximale en middelste derde deel van het bot horizontale schuine fracturen waren met een gemeenschappelijk fractuurgebied in het middelste derde deel van het bot. Met behulp van deze gegevens suggereren we een nieuwe vereenvoudigde classificatie voor scafoïd fracturen; 1) proximale pool fracturen (proximaal ten opzichte van het distale scapholunaat (SL) interval), (2) een bereik van schacht fracturen (met betrekking tot het scaphocapitate (SC) interval), en (3) distale tuberkel fracturen (met betrekking tot het STT-interval).

In **Hoofdstuk 3** is de vereenvoudigde scafoïdfractuur classificatie voor het eerst in gebruik genomen in een databaseonderzoek en een inter-observer onderzoek. Het laat zien dat de vereenvoudigde classificatie gemakkelijk reproduceerbaar is in een grote reeks en fracturen die niet passen in deze classificatie zeldzaam zijn. De aanvullende 'inter-observer' studie vergeleek de vereenvoudigde classificatie met de Herbert-classificatie en toonde een redelijke overeenstemming voor beide classificaties, maar aanzienlijk minder twijfel door de waarnemers bij het classificeren van scafoïd fracturen met behulp van de vereenvoudigde classificatie.

In **Hoofdstuk 4** worden röntgenfoto's en CT-scans gebruikt om proximale pool scafoïd fracturen te diagnosticeren met behulp van een inter-observer onderzoek. De variabiliteit in de diagnose van scafoïd proximale-pool fracturen toonde geen verschil in overeenstemming betreft de diagnose van scafoïd fractuurlocatie met het gebruik van röntgenfoto's alleen of wanneer röntgenfoto's en een CT-scan beschikbaar waren. De betrouwbaarheid was hoog voor beide vormen van beeldvorming. Deze studie suggereert dat een CT-scan de betrouwbaarheid van de diagnose van fractuurlocatie (die bijna perfect is) of verplaatsing van de fractuur (die redelijk is) niet significant verbetert.

In **Hoofdstuk 5** hebben we de overeenstemming getest tussen waarnemers over de mate van botdoorgroei van een midschacht scafoïd fractuur op computertomografie (CT). Waarnemers werd gevraagd om met "het blote oog" het percentage van botdoorgroei te meten. We vonden dat er een matige overeenstemming was over de mate van botdoorgroei van midschacht scafoïd fracturen op CT-scans. Overeenstemming over de locatie van benige overbrugging was gering. We concludeerden dat er beperkte betrouwbaarheid is van het diagnostiseren van locatie en mate van botdoorgroei, en dat hiermee rekening gehouden dient te worden in zowel patiëntenzorg als onderzoek. Wel denken we dat het kwantificeren van de mate van botdoorgroei van invloed kan zijn op het soort en de duur van de behandeling.

In **Hoofdstuk 6** hebben we onderzocht of een arts kan bepalen met behulp van röntgenfoto's en CT-scans of een scafoïd fractuur acuut of oud is. We hebben dit onderzoek verricht omdat er in de praktijk weleens een oude fractuur voor een acute fractuur zal worden aangezien. Dit is belangrijk omdat de behandeling voor oudere en acute fracturen behoorlijk verschillend is. In dit onderzoek bleek de overeenkomst aanzienlijk bij waarnemers die alleen röntgenfoto's bekeken en waarnemers die zowel röntgenfoto's als CT-scans bekeken. We vonden dat onderscheiden van acute fracturen van het scafoïd betrouwbaar is zonder een CT-scan. Het verhaal van de patiënt kan zeker ook van invloed zijn op de interpretatie van beeldvorming.

In **Hoofdstuk 7** werd een nieuwe beeldvormingsmodaliteit de I-Space, een virtual reality-systeem, tot nog toe met name gebruikt in onderzoekssituaties en voor studies van weke delen, getest. De I-Space gebruikt een aparte ruimte met projectoren om de afbeeldingen als een hologram te kunnen bekijken. Wij hebben het gebruikt om moeilijk te diagnosticeren scaphoïd fracturen te analyseren. Resultaten van deze studie suggereren dat de I-Space een modaliteit is met een snelle leercurve en een mogelijk klinisch nut om deze lastige fracturen te beoordelen. Anatomische details kunnen op grote schaal realistisch worden weergegeven, wat resulteert in een zeer illustratief totaalbeeld voor trainingen voor artsen en eventueel pre-operatieve planning.

# PART VI

## ADDENDUM

# Chapter 10

## Tolerance induction via mixed chimerism in vascularized composite allotransplantation: is it time for clinical application?

Current Opinion in Organ Transplantation, 2015
CL Cetrulo Jr, **T Drijkoningen**, DH Sachs

# Abstract

**Purpose of review:** The present review summarizes current data on the induction of immunologic tolerance through mixed hematopoietic chimerism relevant to applying this approach to vascularized composite allotransplantation.

**Recent findings:** Clinical allograft tolerance has been achieved recently for kidney transplants, using nonmyeloablative conditioning regimens and bone marrow transplantation from living donors. The mixed chimerism attained in these studies was either transient or durable, and both permitted tolerance of the renal allografts to be achieved across MHC-matched and MHC-mismatched barriers. In order to extend these protocols to deceased donor transplants across full MHC-mismatched combinations, as will be required for vascularized composite allografts (VCA), a delayed tolerance protocol has recently been developed, in which the donor bone marrow is given 4 months posttransplant. Recent primate studies of kidney transplants using this

protocol have been successful and have demonstrated that strategies to abrogate memory T cells may be helpful.

**Summary:** Induction of tolerance in renal allograft transplantation has been achieved clinically, via mixed chimerism protocols. Modifications of these protocols for transplants, which require use of deceased donors across full MHC mismatches, have shown promise in preclinical models. It is therefore appropriate to consider evaluation of these protocols in clinical trials for kidney transplants, and if successful, for VCA.

**Keywords:** bone marrow transplantation, mixed chimerism, tolerance, vascularized composite allograft

## Introduction

Vascularized composite allotransplantation (VCA) is now an established treatment modality in the management of disfiguring injury, tissue loss, and amputation. Transplantation of VCA, such as the hand, face, or abdominal wall, offers patients remarkable restoration of form and function. The latest report of the International Registry on Hand and Composite

Tissue Transplantation undergoing VCA indicates that these procedures offer patients a significant improvement over conventional reconstruction and/or prostheses with respect to functional outcomes, patient satisfaction, and quality of life.[1,2] However, these significant benefits must be weighed against the risks of long-term immunosuppression required to prevent rejection of VCA, which include infection, malignancy, diabetes, and renal insufficiency.

The induction of immune tolerance of VCA would significantly improve this risk–benefit ratio and would also potentially broaden the indications for vascularized composite transplantation to include, for example, reconstruction following resection of malignant disease or the treatment of congenital anomalies, and permitting novel tissues to be transplanted such as lower extremities, periorbital structures, genitourinary tissue, or smaller complex anatomic units such as digits, ears, lips, or a nose.[3,4] The purpose of this review is to summarize current progress in VCA tolerance strategies and to outline developments in the induction of organ transplant tolerance through hematopoietic chimerism, on which further advances in VCA tolerance will undoubtedly depend.

### Mixed Chimerism

Mixed hematopoietic chimerism, a state in which host-derived and donor-derived hematopoietic cells coexist within an individual after transplantation of donor hematopoietic stem cells from bone marrow (Fig. 1), has led to clinical tolerance for kidneys across MHC matched and mismatched barriers (summarized in the article of Kawai et al.). [3] To achieve mixed chimerism, nonmyeloablative conditioning regimens have been utilized. Mixed chimerism is distinguished from the full (i.e., 100%) chimerism observed after myeloablative conditioning. Mixed chimerism was developed to mitigateagainst graft-versus-host disease and immunoincompetence, frequently seen with full chimerism.[5]

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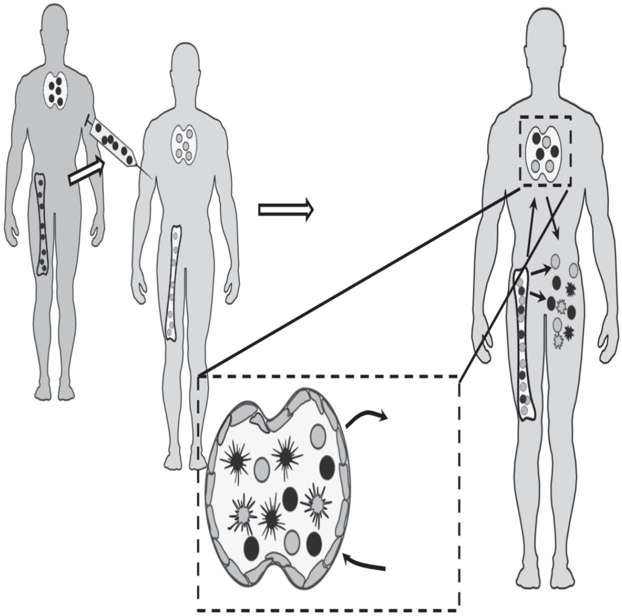

Figure 1. Mixed chimerism donor hematopoietic stem cells (black) are transplanted to the vascularized composite allografts (VCA) recipient (light grey) and migrate to the thymus where both donor and recipient alloreactive cells undergo deletion thereby permitting organ or VCA allograft acceptance.

## The use of the bone marrow stem cell transplantation in clinical vascularized composite allotransplantation

In clinical VCA, bone marrow infusion has been utilized by Dubernard's group in conjunction with face allotransplantation, and by the Pittsburgh/Johns Hopkins group for hand allotransplantation. Dubernard reported no macrochimerism or microchimerism, and it is not clear that a reduction in immunosuppression requirement resulted.[6] Bone marrow infusion used in conjunction with hand transplantation represents an element of the Pittsburgh Protocol, described by Lee et al.[7] In their series, bone marrow infusion 7–21 days post VCA was used as a potential means of preventing graft loss to acute rejection. Skin rejection crises that were observed responded well to topical immunosuppression. The efficacy and safety of their protocol
is not yet clear, and will require long-term followup. No hematopoietic macrochimerism or microchimerism was detected in either of the two patients reported.[7] Nonetheless, the authors suggested that early immunomodulation occurred on the basis of the low levels of maintenance immunosuppression required in these patients. Direct evidence for immunomodulation by a mixed chimerism approach has been reported in a swine model.[8] Despite these data, a protective effect of infused bone marrow effect against VCA rejection was not observed in a recent primate study.[9]

## Clinical renal allotransplantation tolerance protocols

Clinical renal allograft tolerance has been successfully achieved by three centers – MGH, Northwestern, and Stanford – all of which have investigated approaches to induce tolerance using HSCT across HLA-matched or HLA-mismatched kidney transplantation. At MGH, the protocols utilized cyclophosphamide, local thymic irradiation (7 Gy), anti-CD2 mAb, and concomitant kidney and bone marrow transplantation.[10] Patients were maintained on a calcineurin inhibitor for 8- to 14-month posttransplant. All 10 recipients in this protocol developed transient mixed chimerism for 7 to 21 days, and seven were weaned completely from immunosuppression by14 months posttransplantation. Four of the seven successful transplant patients have remained immunosuppression free for 5–12 years, whereas the other three resumed immunosuppression at 5, 7, and 8 years after transplantation due either to recurrence of the original disease or to chronic rejection.[10] In this study, the development of unanticipated de-novo donor-specific antibodies (DSA) was observed, possibly related to the extent of B-cell depletion that resulted from the conditioning regimen. Allograft vasculopathy was not observed, however. The MGH investigators hypothesized that depletion of B cells leads to enhanced B-cell activating factor (BAFF) production, which leads to residual or recovering B-cell activation after transplantation. Addition of rituximab to the regimen prevented denovo DSA production, provided that patients received four doses (DSA formation was not prevented in those patients who received none or two doses).[10] This de-novo production of DSA has not been observed in swine or nonhuman primate models, or has allograft vasculopathy in tolerant animals.[11,12] Further investigation is needed to decipher the relationship between B-cell depletion, BAFF, and de-novo DSA formation and the effect on tolerance. Northwestern University has reported success with induction of tolerance in HLA-mismatched kidney transplant recipients through replacement of recipient hematopoietic cells with donor cells (i.e. full chimerism). Their protocol included total body irradiation (200 Gy), fludarabine (30 mg/kg day 3), and cyclophosphamide (50 mg/kg on day 3). The kidney transplantation took place on day 0 with administration of mycophenolate mofetil and tacrolimus. Donor HSCs combined with 'facilitating cells' produced by a patented enrichment procedure were given on day 1, and cyclophosphamide (50mg/ kg) was administered on day 3. This protocol was designed as a modification of a protocol developed at Johns Hopkins[13] for HLA-mismatched bone marrow transplantation for treatment of hematologic malignancies with reduced risk of GVHD. In this protocol, antihost T cells are suppressed by introducing cyclophosphamide on days 3 and 4 after HSCT. Facilitating cells was added to the Johns Hopkins protocol on the basis of their reported effectiveness in mouse models.[14] Fifteen patients were treated under this protocol, of which nine developed full donor chimerism and in six patients immunosuppression could be discontinued completely.

Longer-term follow-up will be needed to determine the risk–benefit ratio of this

approach.[15]
At Stanford, a total lymphocyte irradiation (TLI)-based regimen has been assessed, utilizing TLI (80–120 cGy, 10 doses total on days 0–9), rabbit antithymocyte globulin (1.5mg/kg, 5 days total on days 0–4), followed by HLA-matched peripheral blood CD34ﬂ stem cell, and CD3ﬂ cell infusion on day 11. Both mycophenolate mofetil and CyA were started on day 0 and lowered over the next 6 months. This regimen achieved success in HLA-matched kidney transplantation in which 19 of 22 patients receiving the protocol developed persistent mixed chimerism, and 16 were weaned completely off immunosuppression. However, this protocol was not successful in HLA-mismatched kidney transplant patients and an attempt to induce stable mixed chimerism and renal allograft tolerance failed. The newest Stanford experimental regimenincludes increased CD34ﬂ cell and CD3ﬂ cell doses is currently being tested.[16-20]

## Advantages of clinical renal transplant tolerance

The results of the MGH tolerance protocol were compared with 21 matched living donor kidney transplant recipients with conventional immunosuppression. During a 10-year period in patients with conventional immunosuppression, four patients lost their kidney grafts from rejection and many suffered posttransplant morbidities, including hypertension requiring medical management (85%), hyperlipidemia (65%), new-onset insulin-dependent diabetes (35%), and serious infectious complications (25%). Comparing this group to the original cohort of patients in whom tolerance was induced, less than half of the recipients are currently on antihypertensive medications and none has developed serious events or malignancies; a good indication can be made that induction of tolerance is useful for sustaining health and graft survival.[10]

## Extension of tolerance protocols to fullmismatches and deseaesed donor transplants; is stable mixed chimerism required?

As mentioned above, extension of these protocols to full MHC-mismatched, deceased-donor combinations will be required for VCA and for many organ allografts other than kidneys. Therefore, an approach to such combinations is currently a major goal in our center and others.
Observations from in-utero models suggested that there may be a need for stable mixed chimerism for nonrenal transplants.[21,22] Consistent with this prediction, and in contrast to preclinical and clinical renal allotransplantation data, in which transient chimerism was sufficient to induce tolerance, stable mixed chimerism was required to achieve tolerance of all components of vascularized composite allografts across a single haplotype mismatch in miniature swine.[11] Stable mixed chimerism and VCA tolerance were achieved across MHC barriers when recipients were previously rendered chimeric, or when treated with simultaneous VCA and chimerism induction.[11] The increased conditioning and resulting toxicity required for achievement of mixed chimerism across a full mismatch

barrier in both swine and primates has led to the development of a delayed tolerance approach in which the allograft is transplanted and donor bone marrow stored at the time of transplant. Primate studies using this protocol for renal allotransplantation have suggested a window for chimerism induction of 4 months posttransplant, when the perioperative inflammatory state has subsided. At this time point, the mixed chimerism-conditioning regimen is initiated and the donor bone marrow given.[12] This approach has been successful in inducing tolerance for MHC-mismatched renal[23] and lung[24] allografts. In the lung study, three of four nonhuman primates became tolerant of their allografts, with two of three tolerant animals exhibiting stable mixed chimerism and the third tolerant animal demonstrating transient chimerism but remaining tolerant of the lung allograft. The two tolerant animals that achieved stable mixed chimerism were transplanted across an MHC-haploidentical mismatch, whereas the animal that developed transient chimerism was transplanted across a higher degree of MHC-matching (two out of four matches at class I, and two out of four matches at class II). A fully MHC-mismatched animal did not exhibit chimerism or tolerance in this study. Nonetheless, this study is particularly exciting as it represents the first demonstration of stable mixed chimerism in a primate chimerism protocol.[24]

## Delayed tolerance and memory

Other recent primate studies have demonstrated that strategies to abrogate allospecific memory T cell (Tmem) responses may be required for clinical tolerance induction using delayed tolerance protocols. In these studies, levels of allospecific Tmem varied significantly between donor–recipient pairs. Interestingly, MHC matching was not always associated with a low memory alloreactivity, with some donor–recipient pairs exhibiting high Tmem alloresponsiveness even with favorable MHC matching and vice versa. Therefore, strategies for selecting donor–recipient pairs with low Tmem alloreactivity may be an important element for the successful induction of tolerance using the delayed tolerance approach.[25-27]

## Mixed hematopoietic chimerism and the skin immune system

The observation of 'split tolerance', in which the host is tolerant of some components of the VCA – that is muscle, bone – but not others (usually skin) has been observed in preclinical VCA experimental models.[28-31] We and others have noted such outcomes, even when stable mixed chimerism was achieved and donor-specific unresponsiveness in invitro assays of peripheral blood-derived leukocytes was evident, suggesting that independent skinspecific mechanisms that escape tolerization through mixed hematopoietic chimerism may be responsible. [29,32,33] Indeed, an appreciation for the complexity of the skin immune system is exemplified by the recent quantification of the T cells in normal, resting human skin, a concentration twice that found in the circulating blood volume.[32,33] T effector and T regulatory populations that permanently reside in the skin have been described and their immune functions characterized in more detail in recent work by Clark and others [34–36]. For example, Langerhans' cells have been shown to modulate local homeostasis by inducing proliferation of skin-resident T regulatory cells under normal conditions or stimulating skin-resident T effector memory cells when exposed to pathogens.[37,38] These new insights underscore the importance of further study of skin-resident immune populations to elucidate mechanisms for tolerance of all components of a VCA, including skin, when mixed chimerism is achieved.

## Conclusion

Induction of tolerance in clinical renal transplantation has been achieved via hematopoietic chimerism approaches. Modification of these successful protocols will be necessary for transplants of VCA that will generally require a deceased donor and a full MHC mismatch. A delayed tolerance approach has shown promise in preclinical models and is ready for evaluation in clinical trials for both renal transplantation and VCA. Further strategies aimed at well-tolerated induction of stable mixed chimerism, including allospecific Tmem suppression and favorable donor–recipient Tmem repertoires are under investigation. In addition, new insights into the unique immunobiology of the skin immune system will be important in future protocols for VCA tolerance.

## References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:
& of special interest
&& of outstanding interest


1. Bertrand AA, Sen S, Otake LR, Lee GK. Changing attitudes toward hand allotransplantation among North American hand surgeons. Ann Plast Surg 2014; 72:S56–S60.
2. Khalifian S, Brazio PS, Mohan R, et al. Facial transplantation: the first 9 years. Lancet 2014; 384:2153–2163.
3.&& Kawai T, Leventhal J, Madsen JC, et al. Tolerance: one transplant for life. Transplantation 2014; 98:117–121. Summarizes issues discussed at the first international workshop for clinical tolerance: protocol consensus, clinical recommendations, and ongoing research topics.
4. Leonard DA, Kurtz JM, Cetrulo CL Jr. Achieving immune tolerance in hand and face transplantation: a realistic prospect? Immunotherapy 2014; 6:499–502.
5. Sachs DH, Kawai T, Sykes M. Induction of tolerance through mixed chimerism. Cold Spring Harb Perspect Med 2014; 4: a015529.
6. Petruzzo P, Dubernard JM. The International Registry on Hand and Composite Tissue allotransplantation. Clin Transpl 2011; 247–253.
7. Schneeberger S, Gorantla VS, Brandacher G, et al. Upper-extremity transplantation using a cell-based protocol to minimize immunosuppression. Ann Surg 2013; 257:345–351.
8.&& Leto Barone AA, Shanmugarajah K, Leonard DA, Kurtz JM, Albritton A, et al. Effects of transient donor chimerism on rejection of MHC-mismatched vascularized composite allografts in swine. Vasc Compos Allotransplant 2015; 1: 1, 1-8, DOI: 10.1080/23723505.2015.1039692. Large animal data suggesting transient chimerism has an immunomodulatory effect but is not adequate for full VCA tolerance.
9.&& Brazio PS, Woodall J, Panda A, et al. Infused bone marrow fails to prevent vascularized composite allograft rejection in nonhuman primates. Am J Transplant 2015; 15:2011–2012. Primate study suggesting that infused bone marrow does not have a protective effect against VCA rejection.
10. &&Kawai T, Sachs DH, Sprangers B, et al. Long-term results in recipients of combined HLA-mismatched kidney and bone marrow transplantation without maintenance immunosuppression. Am J Transplant 2014; 14:1599–1611. Reports long-term results of 10 recipients who received combined kidney and bone marrow transplantation.
11. &&Leonard DA, Kurtz JM, Mallard C, et al. Vascularized composite allograft tolerance across MHCbarriers in a large animal model. Am J Transplant 2014; 14:343–353. Swine model achieved VCA tolerance across a haploidentical mismatch.
12. Yamada Y, Benichou G, Cosimi AB, Kawai T. Tolerance induction after organ transplantation, “delayed tolerance” via the mixed chimerism approach: planting flowers in a battle field. Chimerism 2012; 3:24–28.

13. Bolanos-Meade J, Fuchs EJ, Luznik L, et al. HLA-haploidentical bone marrow transplantation with posttransplant cyclophosphamide expands the donor pool for patients with sickle cell disease. Blood 2012; 120:4285–4291.
14. Huang Y, Bozulic LD, Miller T, et al. CD8afl plasmacytoid precursor DCs induce antigen-specific regulatory T cells that enhance HSC engraftment in vivo. Blood 2011; 117:2494–2505.
15. Leventhal J, Abecassis M, Miller J, et al. Chimerism and tolerance without GVHD or engraftment syndrome in HLA-mismatched combined kidney and hematopoietic stem cell transplantation. Sci Transl Med 2012; 4:124ra28.
16. Strober S, Dhillon M, Schubert M, et al. Acquired immune tolerance to cadaveric renal allografts. A study of three patients treated with total lymphoid irradiation. N Engl J Med 1989; 321:28–33.
17. Strober S, Benike C, Krishnaswamy S, et al. Clinical transplantation tolerance twelve years after prospective withdrawal of immunosuppressive drugs: studies of chimerism and antidonor reactivity. Transplantation 2000; 69:1549–1554.
18. Saper V, Chow D, Engleman ED, et al. Clinical and immunological studies of cadaveric renal transplant recipients given total-lymphoid irradiation and maintained on low-dose prednisone. Transplantation 1988; 45:540–546.
19. Millan MT, Shizuru JA, Hoffmann P, et al. Mixed chimerism and immunosuppressive drug withdrawal after HLA-mismatched kidney and hematopoietic progenitor transplantation. Transplantation 2002; 73:1386–1391.
20. Millan MT, Shizuru SJ, Lowsky J, et al. Studies of tolerance and chimerism after combined blood stem cell and kidney transplantation in humans. Am J Transplant 2005; 5:544.
21.&& Mathes DW, Solari MG, Gazelle GS, et al. Stable mixed hematopoietic chimerism permits tolerance of vascularized composite allografts across a full major histocompatibility mismatch in swine. Transpl Int 2014; 27:1086– 1096. An in-utero swine model was utilized to achieve induction of VCA tolerance across a full major histocompatibility mismatch, demonstrating that stable mixed chimerism is sufficient for VCA tolerance.
22. Vrecenak JD, Pearson EG, Santore MT, et al. Stable long-term mixed chimerism achieved in a canine model of allogeneic in utero hematopoietic cell transplantation. Blood 2014; 124:1987–1995.
23. Benichou G, Nadazdin O, Cosimi AB, Kawai T. Successful tolerance to fully MHC disparate renal allografts via donor hematopoietic mixed chimerism in nonhuman primates. Am J Transplant 2013; 13:2500.
24.&& Tonsho M, Lee S, Aoyama A, et al. Tolerance of lung allografts achieved in nonhuman primates via mixed hematopoietic chimerism. Am J Transplant 2015; 15:2231–2239. Tolerance to lung allografts in primates achieved by stable mixed chimerism.
25. Yamada Y, Boskovic S, Aoyama A, et al. Overcoming memory T-cell responses for induction of delayed tolerance in nonhuman primates. Am J Transplant 2012; 12:330–340.
26. Nadazdin O, Boskovic S, Murakami T, et al. Host alloreactive memory T cells influence tolerance to kidney allografts in nonhuman primates. Sci Transl Med 2011; 3:86ra51.

27. Lee S, Yamada Y, Tonsho M, et al. Alefacept promotes immunosuppressionfree renal allograft survival in nonhuman primates via depletion of recipient memory T cells. Am J Transplant 2013; 13:3223–3229; Oct 24.
28. Lee WP, Rubin JP, Cober S, et al. Use of swine model in transplantation of vascularized skeletal tissue allografts. Transplant Proc 1998; 30:2743– 2745.
29. Mathes DW, Randolph MA, Solari MG, et al. Split tolerance to a composite tissue allograft in a swine model. Transplantation 2003; 75:25–31.
30. Horner BM, Randolph MA, Duran-Struuck R, et al. Induction of tolerance to an allogeneic skin flap transplant in a preclinical large animal model. Transplant Proc 2009; 41:539–541.
31. Hettiaratchy S, Melendy E, Randolph MA, et al. Tolerance to composite tissue allografts across a major histocompatibility barrier in miniature swine. Transplantation 2004; 77:514–521.
32. Clark RA, Watanabe R, Teague JE, et al. Skin effector memory T cells do not recirculate and provide immune protection in alemtuzumab-treated CTCL patients. Sci Transl Med 2012; 4:117ra7.
33. Jiang X, Clark RA, Liu L, et al. Skin infection generates nonmigratory memory CD8fl T(RM) cells providing global skin immunity. Nature 2012; 483:227– 231.
34. Di MP, Perera GK, Nestle FO. The multitasking organ: recent insights into skin immune function. Immunity 2011; 35:857–869.
35. Tay SS, Roediger B, Tong PL, et al. The skin-resident immune network. Curr Dermatol Rep 2014; 3:13–22.
36. Seneschal J, Clark RA, Gehad A, et al. Human epidermal Langerhans cells maintain immune homeostasis in skin by activating skin resident regulatory T cells. Immunity 2012; 36:873–884.
37. Bennett CL, Fallah-Arani F, Conlan T, et al. Langerhans cells regulate cutaneous injury by licensing CD8 effector cells recruited to the skin. Blood 2011; 117:7063–7069.
38. Kaplan DH. In vivo function of Langerhans cells and dermal dendritic cells. Trends Immunol 2010; 31:446–451.

# Epilogue

With great honor, I write this epilogue acknowledging this revealing Thesis and the tremendous scholarly efforts of Dr Tessa Drijkoningen. The title of this Thesis elegantly reflects Tessa's passionate and exhaustive quest for answers on a topic that remains a challenge today: What's the secret behind a reliable diagnosis and classification of scaphoid fractures? Through the combination of some of the most advanced techniques including 3D fracture pattern analysis techniques and a 3D I-space model with an immense panel of reviewing collaborators, Tessa managed to establish solid evidence important in improving treatment of patients with scaphoid fractures.

Although this Thesis could stand alone as a tribute to Dr. Drijkoningen's solid scientific efforts and achievements, it doesn't reflect her full academic investigation. In fact, her kindness and humble appearing may haze her secret power and fierce dedication to scientific innovation. In her quest, Tessa has gone far beyond the data of this Thesis. Undaunted by any complexity and controversy, she has played a remarkable role in the advancement of hand transplantation. I greatly admire her courage to help advance this potentially highly valuable field of medicine and I hope that her contagious levels of scientific enthusiasm will improve success rates and outcome of future hand transplantions in the Netherlands and around the world.

Geert A. Buijze, MD PhD
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As father and geophysicist, I have followed Tessa with keen interest, of course. Before Tessa started with this research, I had never heard of scaphoid fractures, but I was intrigued by the images used for her analysis. In geophysics, 2D and 3D images are central to an understanding of the earth, and in medical imaging it is not different, only the object is different. I am always impressed what is possible in medical imaging, which often has the advantage that you can measure around the object. Similar to geophysics, you can do all types of analyses on the images, like Tessa has done in this thesis, including 3D analyses, fracture mapping and virtual reality. As father I am of course impressed by her producing such a nice booklet which, I hope, will be used within the scaphoid-fracture community.

It is always a challenge to do a PhD, with the ups and downs. Tessa made a good start in Boston but did a lot of the work for the thesis while she was also working as ANIOS in different hospitals in The Netherlands. It really shows her determination and perseverance to get it all done, which is characteristic of her personality. This work shows she has become an even better physician by including the research skills to analyse patients. And this all next to her existing qualities for being a good physician, namely taking up responsibilities, searching for solutions, being a good organiser, a good listener, an empathic and sociable person.

Guy G. Drijkoningen, Dr. Ir.
Associate Professor Applied Geophysics
Delft University of Technology

# Thanks and Recognition

I would love to thank my **parents** for teaching me passion and discipline which brought me to this point in life. It also made me a persistent researcher who knew she could manage living in the United States by herself.

Love you to the moon and back!

My **'sister' Danielle** took the chance to visit Boston and the NY Fashion week in 2015. The days we spent together were unforgettable and you became even more dear to me from that moment on!

Great thanks to **Eelke**, the love of my life, to help me through good and bad times.

Life wouldn't be the same without you.

Dear **Uncle Rob**, special thanks to you for your support making this adventure possible for me by supporting my stay in Boston for 2 years.

My dearest best friend and paranimf Annika, special thanks to you to always be there for me. Hope I will have the honour to stay in your life till the end of times.
Ekin and me started off in 'het Vlietland Ziekenhuis' were we both worked as general surgery junior residents. You thought I was 'the bitch of the surgery department' but we soon became very good friends. You are so relaxed and funny, hope we will be collegues again soon.

Corey, what more can I say. You made my time in Boston the greatest of my life!
I enjoyed all our great trips and adventures, like the NY Fashion Week, Bill Board Awards etc. Besides that you are really the one that taught me to 'think out of the box', which was helpful for this thesis but is especially a valuable life lesson.

Thanks to my fellow researchers at
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Yvonne Braun, Bianca Verbeek, Bart Lubbers, Jos Mellema, Teun Teunis, Stein Jansen, Wouter van Leeuwen, Kamil Ofazoglu, Quirine van der Vliet, Susanne Wilkens, Marijn van Berckel and Andrea Stephanie van der Heijden.

**David Ring** was my main supervisor for this thesis. He taught me to structure the jungle called 'medical research'. Great thanks for mentoring me during this thesis and making me part of the Science Factory.

**Geert**, friend and co-promotor of this thesis. Dr Strackee once called me 'the female version of Geert'. It felt like an honor being compared to you. Your ongoing motivation and drive inspired me to move on and never give up. It led to this thesis and to future hunger trying to make the impossible possible.

I would love to thank **Curtis L Cetrulo jr** for working with me on his transplant projects and making me passionate about his life-work.
I will keep fighting to make our shared passion into a great transplant project here in the Netherlands!

**The Massachusetts Medical Society Alliance** where I became vice-president after 3 months in Boston. I'm very grateful meeting all these inspiring and influencing people and to have a taste of charity work in the United States.
Especially Yvonne, my very open-minded collegue and dear friend, who was my 'closet' companion at MGH.
You taught me to find solutions which might not be the most obvious.

## Scientific Output (other than this thesis)

### *Articles*

**Drijkoningen T**, Beeres FJP, van Leerdam RH, Grootendorst DC, Rhemrev SJ. Functional outcome in conservatively treated non-displaced scaphoid fractures. *Open Journal of Clinical Diagnostics, 2012, http://www.scirp.org/*

**Drijkoningen T**, Peters R, Eberlin KR, Mudgal CS, Cetrulo CL Jr. Case study: Osteosynthesis, tenodesis effect and side-to-side tendon repair in hand transplantation. *Tech Hand Up Extrem Surg. 2015 Jul 18*

**Drijkoningen T**, van Weel V, Eberlin KR, Cetrulo CL Jr. Eptifibatide salvage of arterial anastomotic thrombosis in lower extremity free flap reconstruction: a case report. *J Reconstr Microsurg. 2015 Sep;31(7):544-6*

**Drijkoningen T**, van Berckel M, Becker SJE, Ring DC, Mudgal CS Night Splinting for Idiopathic Trigger Digits. *Hand NY. 2017 Aug 1:1558944717725374. doi: 10.1177/1558944717725374*

Meijer SJ, Janssen SJ, **Drijkoningen T**, Ring DC. Factors associated with failure of primary surgery of perilunate dislocations. *J Wrist Surg. 2015 May; 4(2):88-92*

Moradi A, Kachooei A, **Drijkoningen T**, Ring DC. Factors associated with re-operation after surgery for scaphoid nonunion. *The Journal of Hand Surgery. 2015 Sept; Volume 40, Issue 9, Supplement, Page 10*

Oh A, **Drijkoningen T**, Menendez ME, Ring DC. The Relation of Psychological Factors to the Michigan Hand Questionnaire. *Hand NY. 2016, March; doi: 10.1177/1558944716642765*

Ten Berg P, **Drijkoningen T**, Guitton T, Ring DC, Strackee SD, SOVG. Does a Comparison View Improve the Reliability of Staging Wrist Osteoarthritis? *Hand NY. 2017 Sep;12(5):439-445. doi: 10.1177/1558944716677541.*

Ng ZY, Lellouch AG, **Drijkoningen T**, Chang IA, Sachs DH, Cetrulo CL Jr. Vascularized Composite Allotransplantation-An Emerging Concept for Burn Reconstruction. *J Burn Care Res. 2017 Nov/Dec;38(6):371-378. doi: 10.1097/BCR.0000000000000532.*

***Bookchapter***

**Drijkoningen T**, ten Berg P. Scaphoid Fractures: Evidence-Based Management. Chapter 8 "Classification Systems of Scaphoid Fractures". Jesse B. Jupiter and Geert A. Buijze (2017, Elsevier).

***Presentations***

**Drijkoningen T**, Beeres FJP, Knotter R, Thomassen B, Rhemrev SJ. I-space: Future in the diagnostics of scaphoid fractures? *TOWN conference 2013 (The Hague)*

**Drijkoningen T**, Beeres FJP, De Deckere E, Grootendorst DC, Rhemrev SJ. Hand strength measurement is not useful in the diagnostic work-up of carpal fractures. *Istanbul EFORT 2013*

**Drijkoningen T**, Strackee SD, Mudgal CS, Eberlin K, Winograd J, Cetrulo CL Jr. Handtransplantatie; status van een casus 3 jaar post-operatief. *Nederlandse Vereniging voor Plastische Chirurgie, Jaarvergadering oktober 2015*

**Drijkoningen T**, van Leeuwen WF, Claessen FM, Ring DC. Demographics associated with acute tubercle, waist and proximal pole fractures of the scaphoid. *NEHS 2015*

**Drijkoningen T**, Guitton T, Rakhorst H; Opzetten interobserver platvorm voor "Nederlandse Vereniging voor Plastische Chirurgie". *NVPC voorjaarsvergadering 2017*

**Drijkoningen T**, Ten Berg P, Buijze GA, Guitton T, Ring DC, SOVG. Is the quantification of partial union of scaphoid fractures on computed tomography reliable? *NVPC voorjaarsvergadering 2017 and Smith Day april 2017*

Ng ZY, Lellouch A, **Drijkoningen T,** Sachs DH, Cetrulo CL Jr,. Vascularized allotransplantation in burnwound patients; an overview.
*Annual Meeting in Boston 2017*

D Young-Afat, **Drijkoningen T**, WKNVPC. Opti-Flapp and interobserver platform in the Netherlands. *Reconstructive Surgery Trials Network (RSTN), june 2017*

**Drijkoningen T,** Guitton T, Strackee SD, Ring DC, SOVG. Identificatie en classificatie van scaphoid fracturen. *NVPC voorjaarsvergadering 2018*

### *Posters*

**Drijkoningen T**, Beeres FJP, Grootendorst DC, Rhemrev SJ. Physical examination in scaphoid fractures; hematoma, scaphoid compression test, tender anatomical s nuffbox and radial compression. *Istanbul EFORT 2013*

Holzer P, Schol I, **Drijkoningen T**, Tanrikut C, Ko DSC, Cetrulo CL Jr. Strategizing genitourinary vascularized composite allotransplantation: Deceased donor allograft procurement.
*Fort Lauderdale Military Health System Research Symposium 2015, poster*

### *Transplant Protocols*

Austen WG, Cetrulo CL Jr., Colwell AS, **Drijkoningen T**, Jupiter JB, Ko DS, Kontos NJ, Kotton CN, Liao E, Madsen JC, Markmann J, Mudgal CS, Patel VI, Ring DC, Sachs DH, Schol I, Spitzer TR, Warren L, Winograd JM, Yaremchuk MJ

- Delayed tolerance induction in upper extremity allotransplantation (approved)
- Genito-urinarytract transplantation (approved and applied)
- Face transplantation (approved)

## About the Author

After her birth in Cambridge (United Kingdom) during her fathers PhD-period, Tessa grew up in Delft in a small loving family (The Three Musketeers). In 2006 she started studying Medicine at Leiden University and became a member of Augustinus, where she met her lovely friends of Blitz.

As Tessa loves traveling and adventure, during summer-breaks she went to a rehabilitation clinic in Cape Town (South Africa; 2007), to a private hospital in Adepazzari (Turkey; 2008) and just before starting her internships she went to the Academical Hospital Paramaribo (Suriname; 2010) to get ready being a docter.

She started her career as general surgery resident at Vlietland Ziekenhuis in Schiedam. One day she sat down with Steven Rhemrev, traumatologist HMC, to talk about her future plans and had the privilege to be connected to David Ring in Boston. After Davids' quick e-mail approval and loads of paperwork, 8 months later Tessa started an unforgettable journey to Boston where she lived for nearly 2 years.

In Boston Tessa was a researcher at the Hand and Upper-Extremity Service, but as she had that secret love for plastic surgery she applied as clinical researcher at the Plastic and Reconstructive Surgery Department at Massachusetts General Hospital with Dr CL Cetrulo Jr. This is where her passion and future goals in Vascularised Allo-Transplant Surgery were born. In this department she had the honor to publish two articles with David Sachs, a world-respected immunologist. Besides her work in the hospital Tessa became vice-president of the Massachusetts Medical Society Alliance (MMSA) and helped organizing charity events and met a lot of amazing, inspiring and world influencing people.

Getting foot on the ground in The Netherlands in 2016  Tessa went working as a ‘traveling’ resident in Plastic and Reconstructive Surgery in ‘het Amphia Ziekenhuis’ in Breda, ‘het Zuyderland Ziekenhuis’ in Heerlen and in the 'Catharina Ziekenhuis/ Maxima Medisch Centrum/St Anna Ziekenhuis' in the Eindhoven region. She is currently working as gender-surgery resident in the Plastic Surgery Department at the 'VU medical center' in Amsterdam, where she is currently living with her loving Eelke.

Amsterdam Movement Sciences

Amsterdam Movement Sciences conducts scientific research to optimize physical performance in health and disease based on a fundamental understanding of human movement in order to contribute to the fulfillment of a meaningful life.