Evolution in Peripheral Nerve Repair: The Use of Processed Nerve Allograft

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Stanford MEDICINE

T B C SINCE 1970

UCSF University of California San Francisco

Disclosures

- Axogen
  - Research grant recipient
  - Consultant

HARRY J. BUNCKE (1922-2008)

BUNCKE

BUNTIC

SAFA

WATT



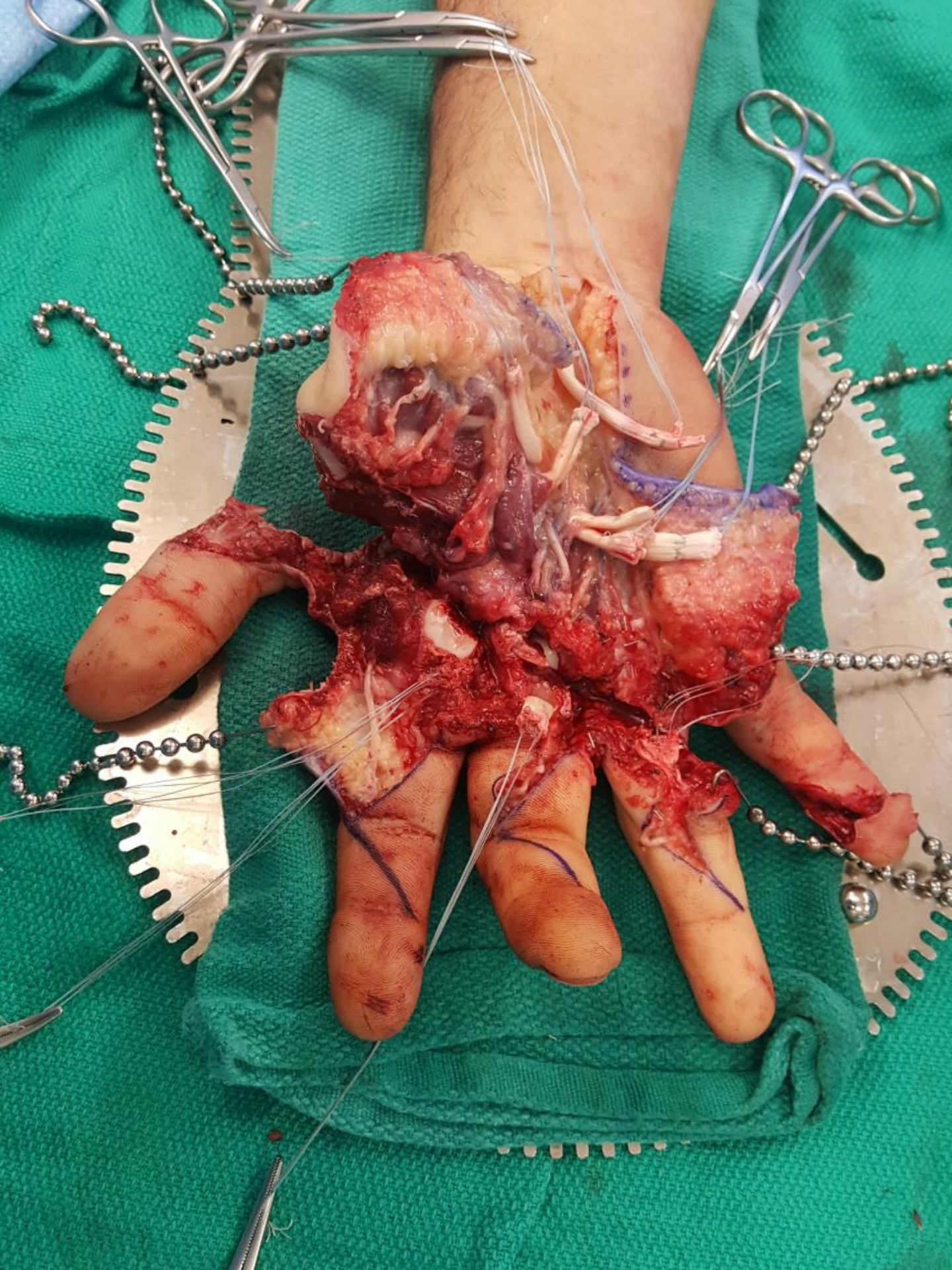







Agenda

- How we started using nerve allografts
- Sensory cases
- Motor cases
- RANGER data
- MATCH data



Options at the time

- Nerve conduit (mostly collagen)
- Autograft
  - Close up
  - Return a few months later
  - Resect
  - Graft

Conduits

- Our experience did not mirror the “Weber Study”
  - Gaps > 1cm did not seem to perform well

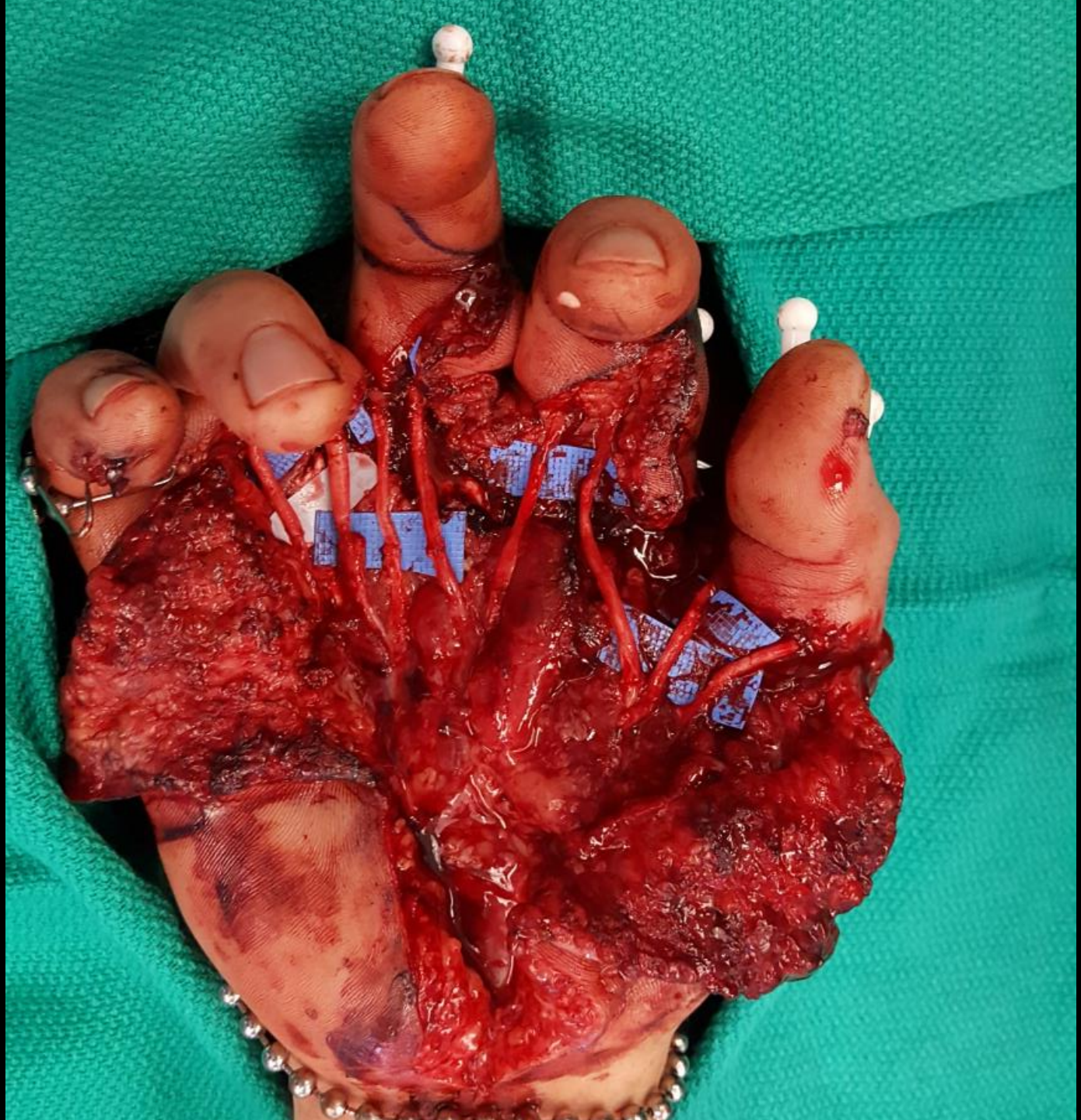
Existing Data for Nerve Conduits

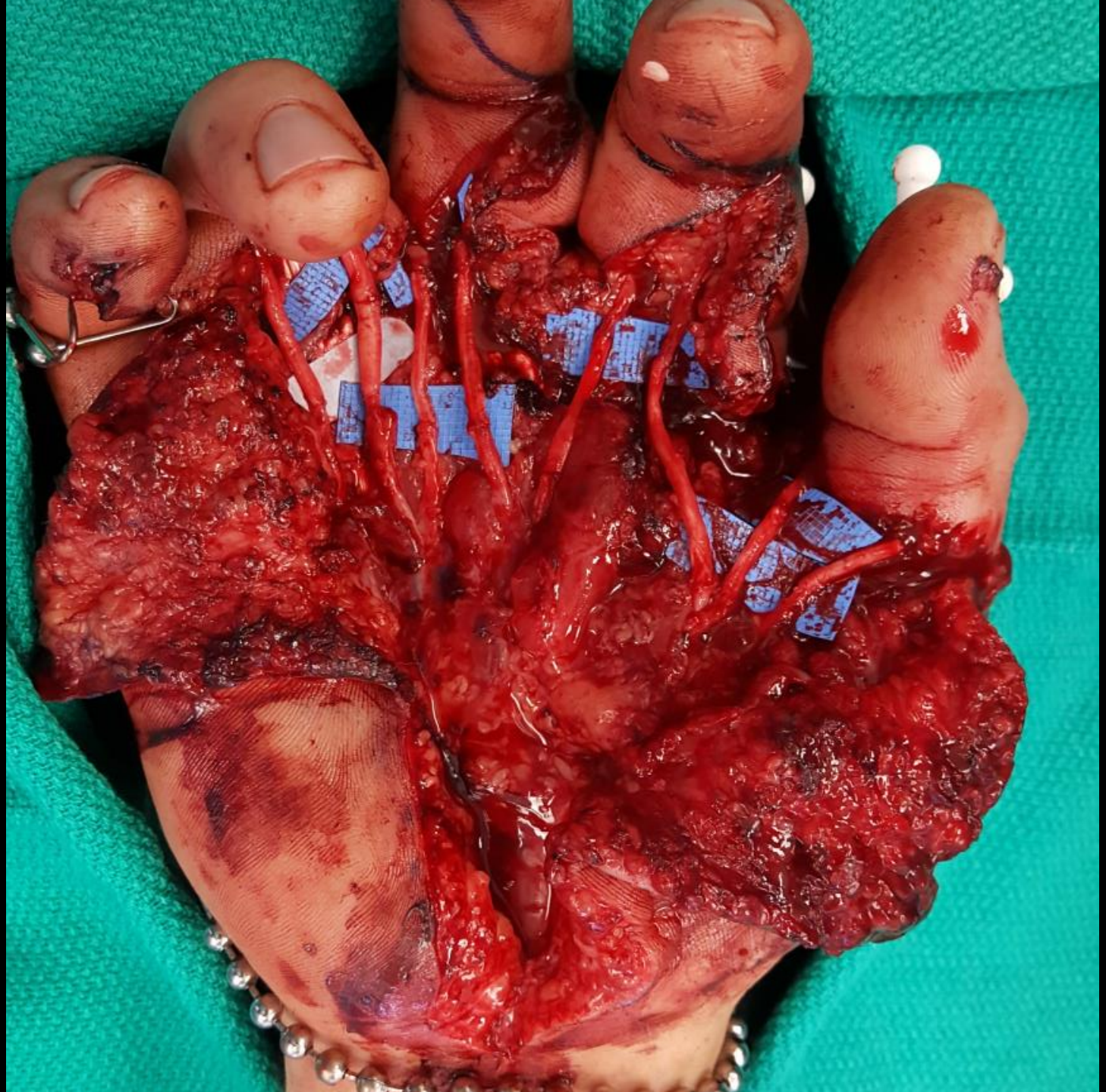
- Weber et al 2000, PGA tube
  - First and only randomized prospective multi-center study on conduits
    - 126 Nerves Injuries in 98 Subjects
    - 25% of injuries lost to follow-up
    - 46 nerves treated with conduits evaluated
  - Compared outcomes to 2 control groups Direct Repair and Autograft
  - Repairs in the hand distal to the SPA
  - Recovery assessment of 2-PD (moving or static which ever was lower)
  - Mean gap length = 7 mm; Maximum conduit length = 25 mm
  - Length of 30 mm not tested with conduits

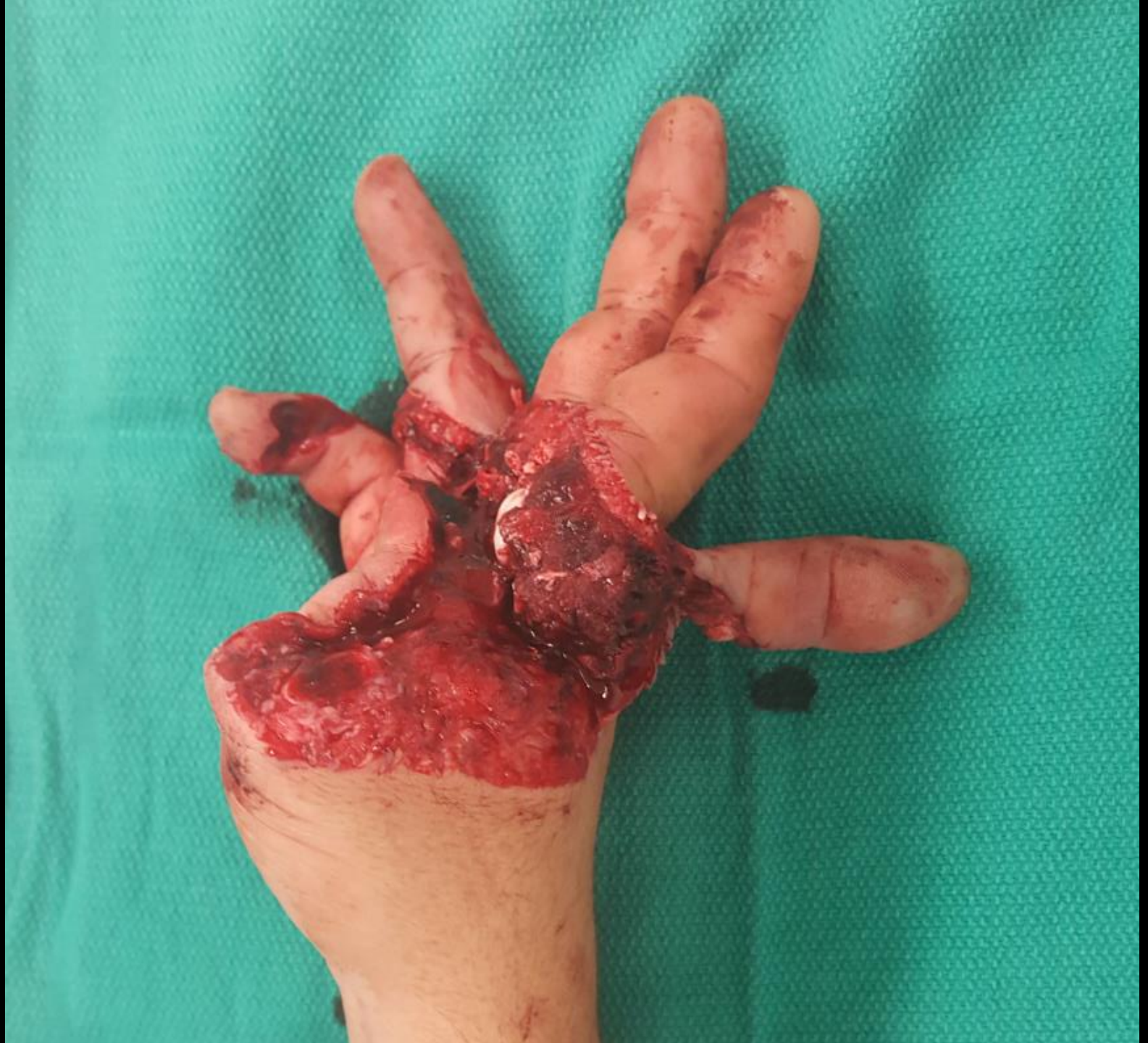
Conduit

Recovery	*Gap ≤ 4mm*	*Gap 5-7mm*	*Gap ≥ 8mm*	*Total*
Excellent	*10(91%)*	*3 (17%)*	*7 (42%)*	*20*
Good	*1 (9%)*	*8 (44%)*	*5 (29%)*	*14*
Poor	*0*	*7 (39%)*	*5 (29%)*	*12*
Total	*11*	*18*	*17*	*46*


Back to our case…







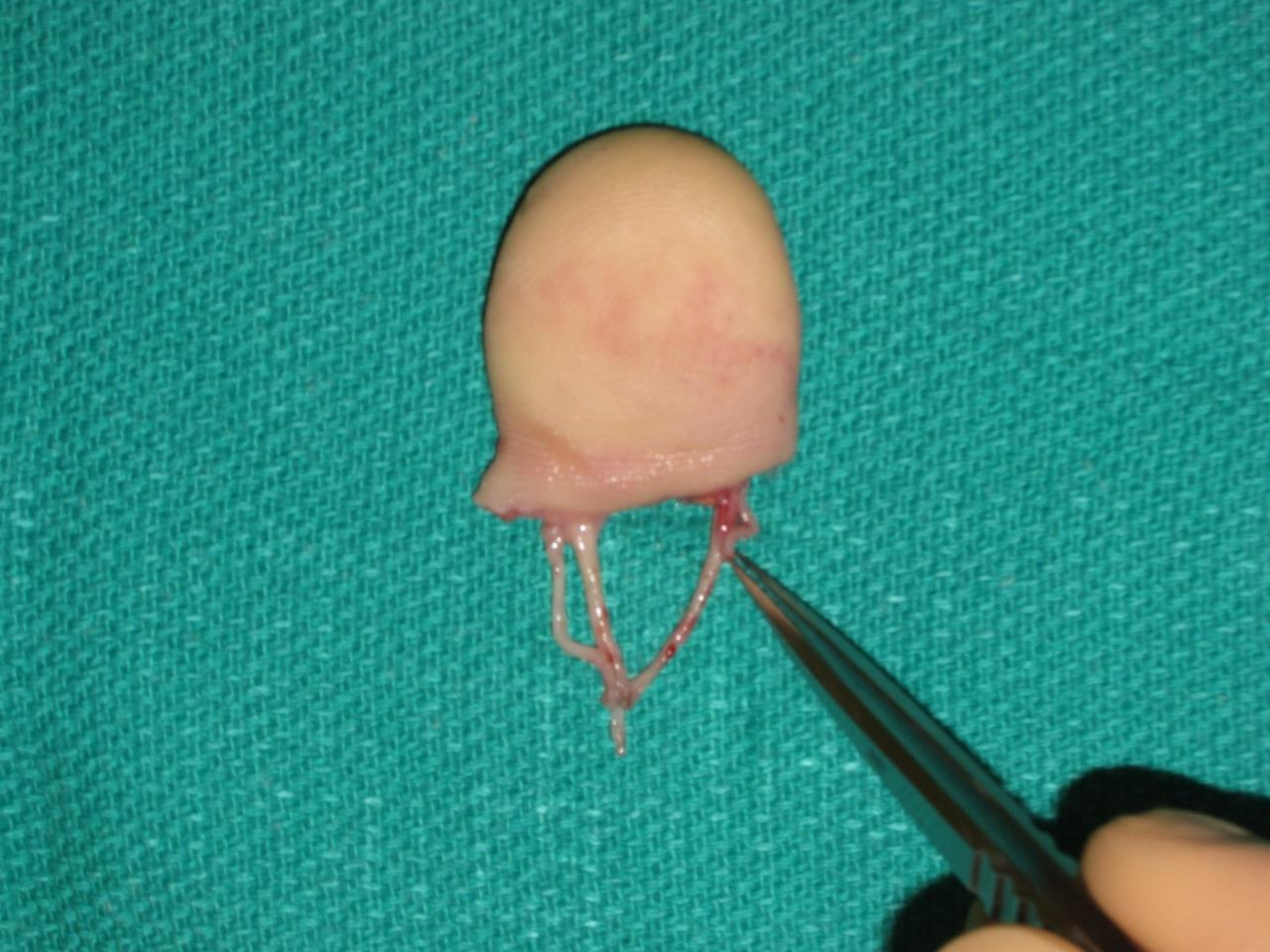

3 Months Post-Op


3 Months Post-Op


3 Months Post-Op


3 Months Post-Op

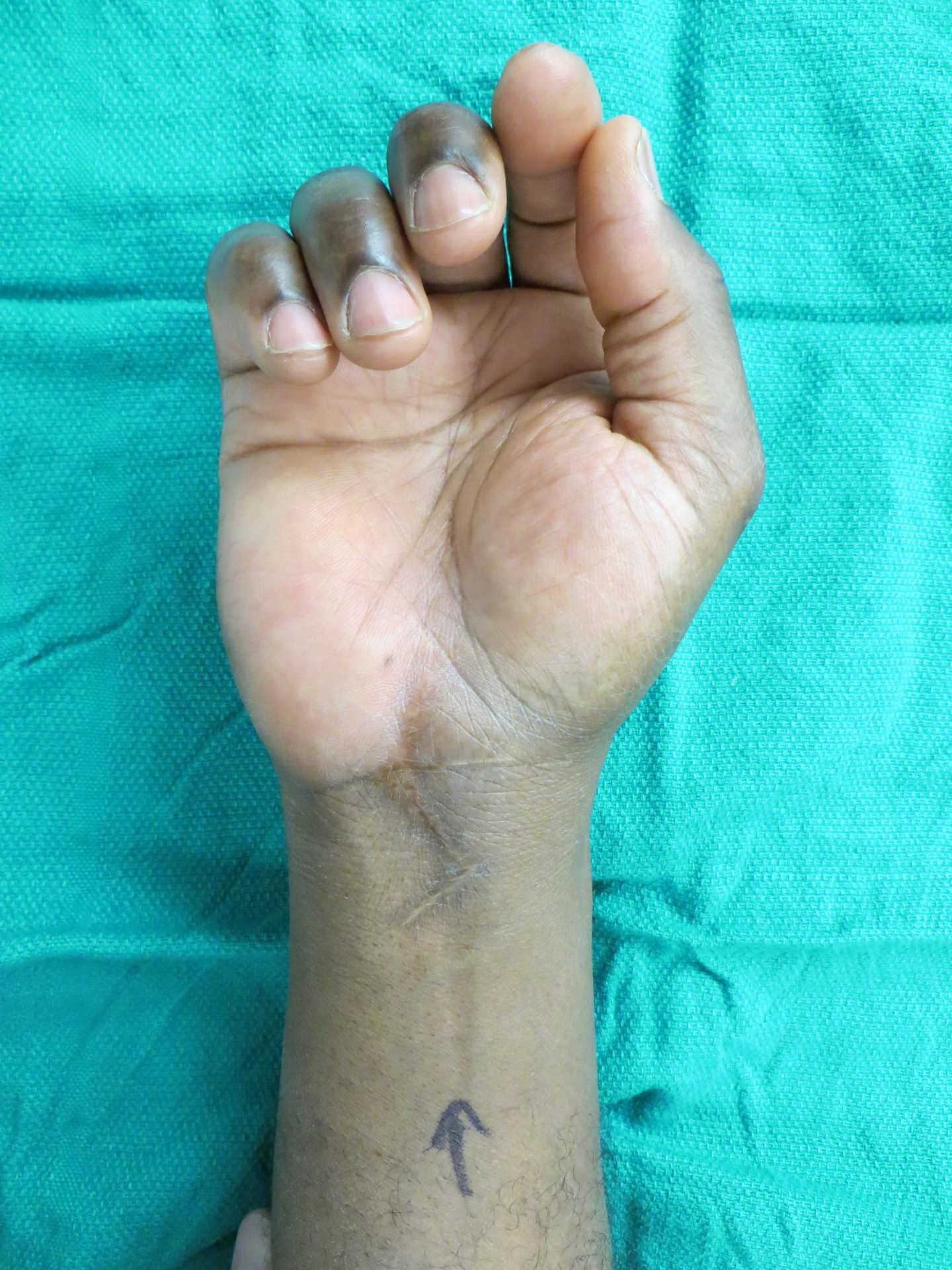
THUMB AVULSION AMPUTATION

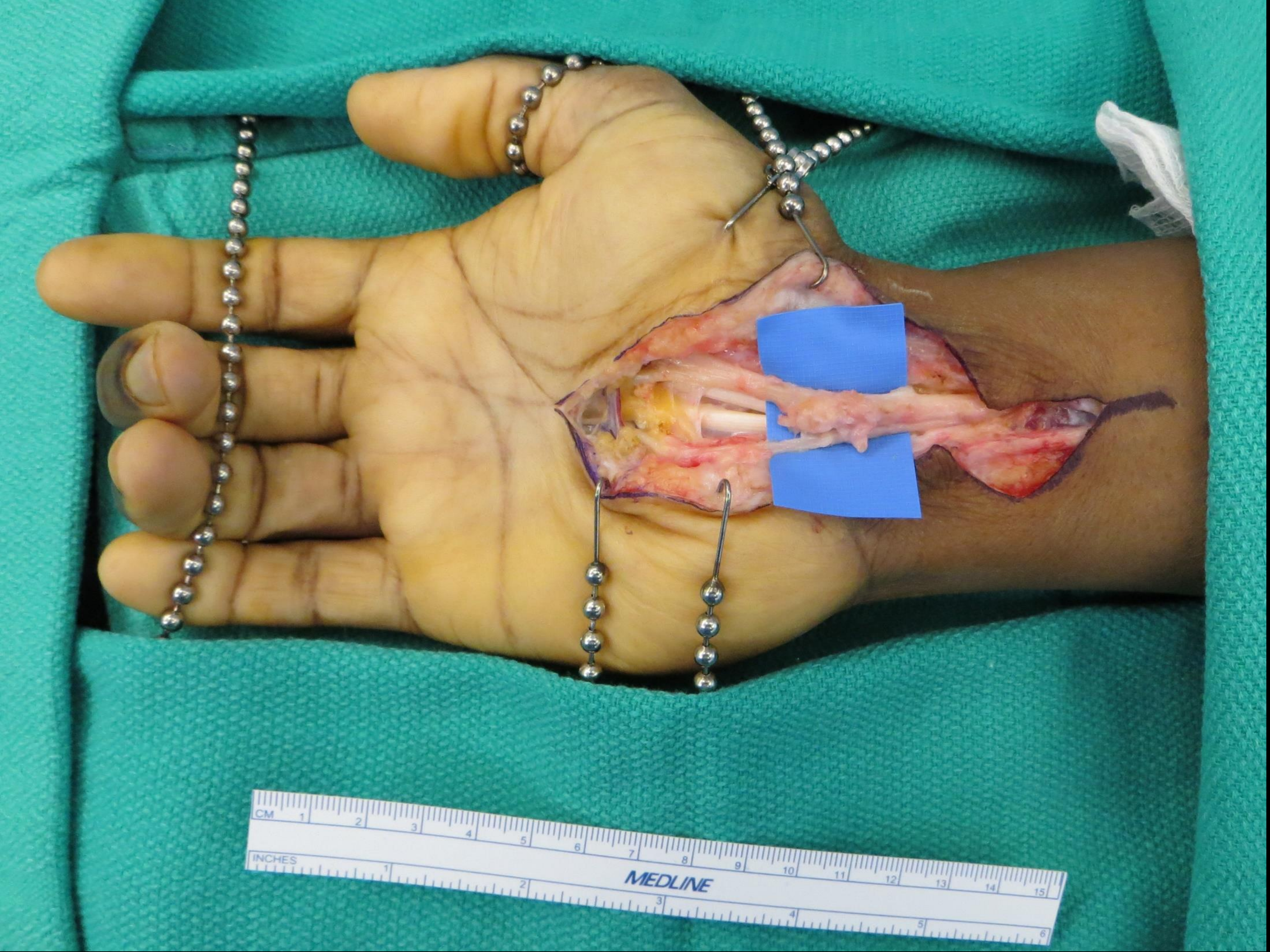


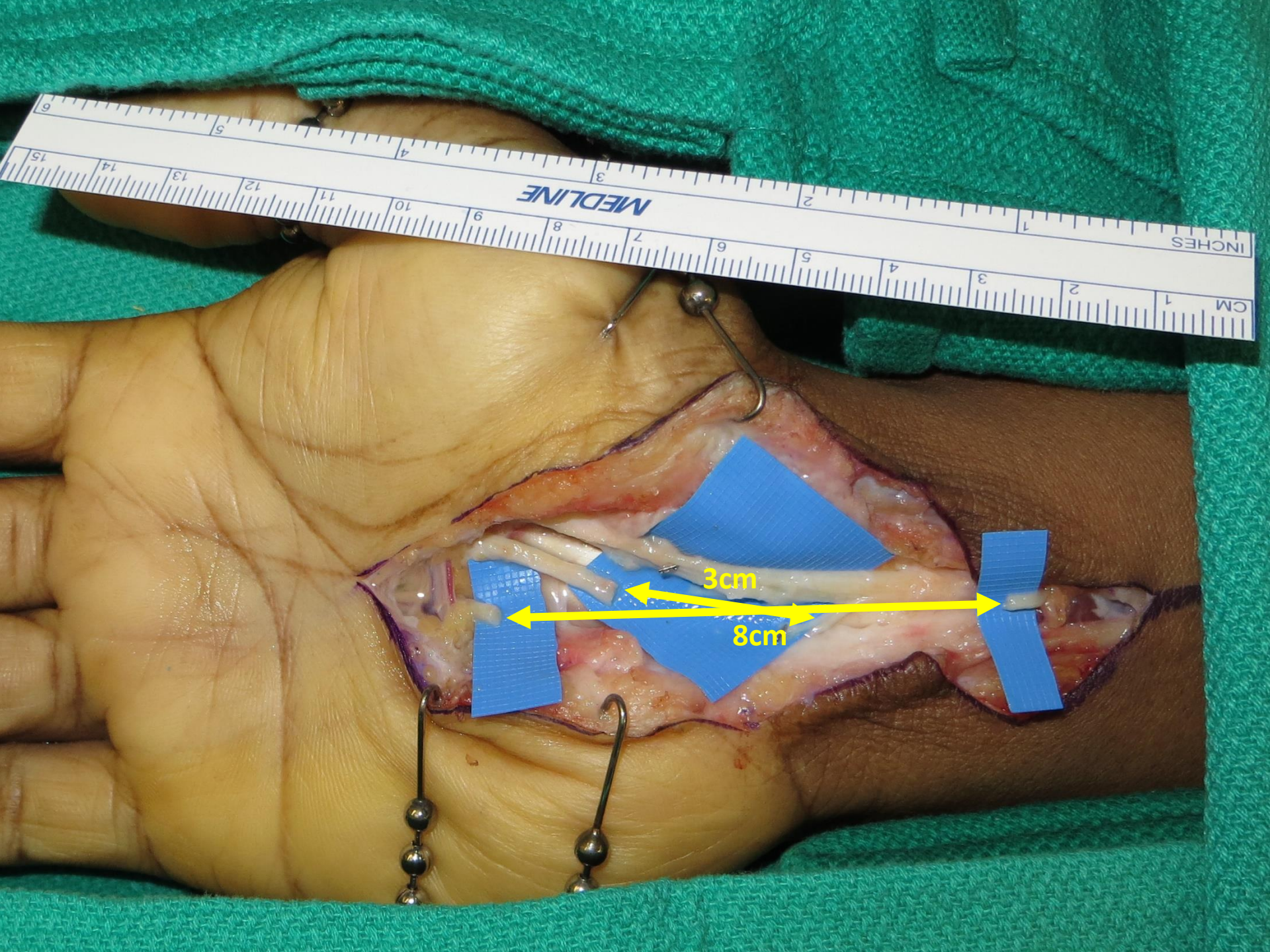

RDN: 4cm Nerve Allograft
UDN: 4cm Nerve Allograft

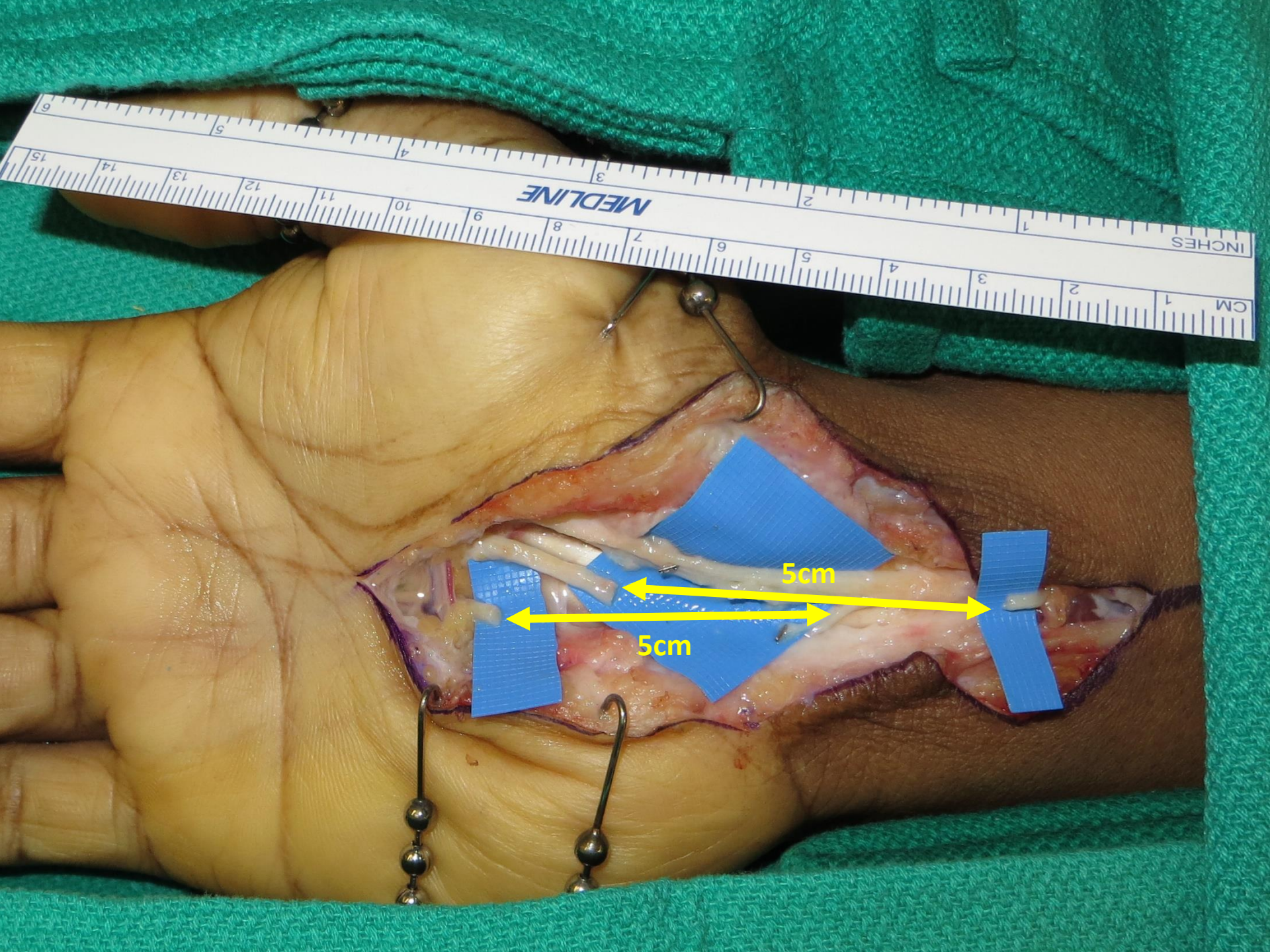

RDN: SWMF 3.61 (0.4g)
S2PD 8 mm
UDN: SWMF 4.31 (2g)
S2PD 12mm

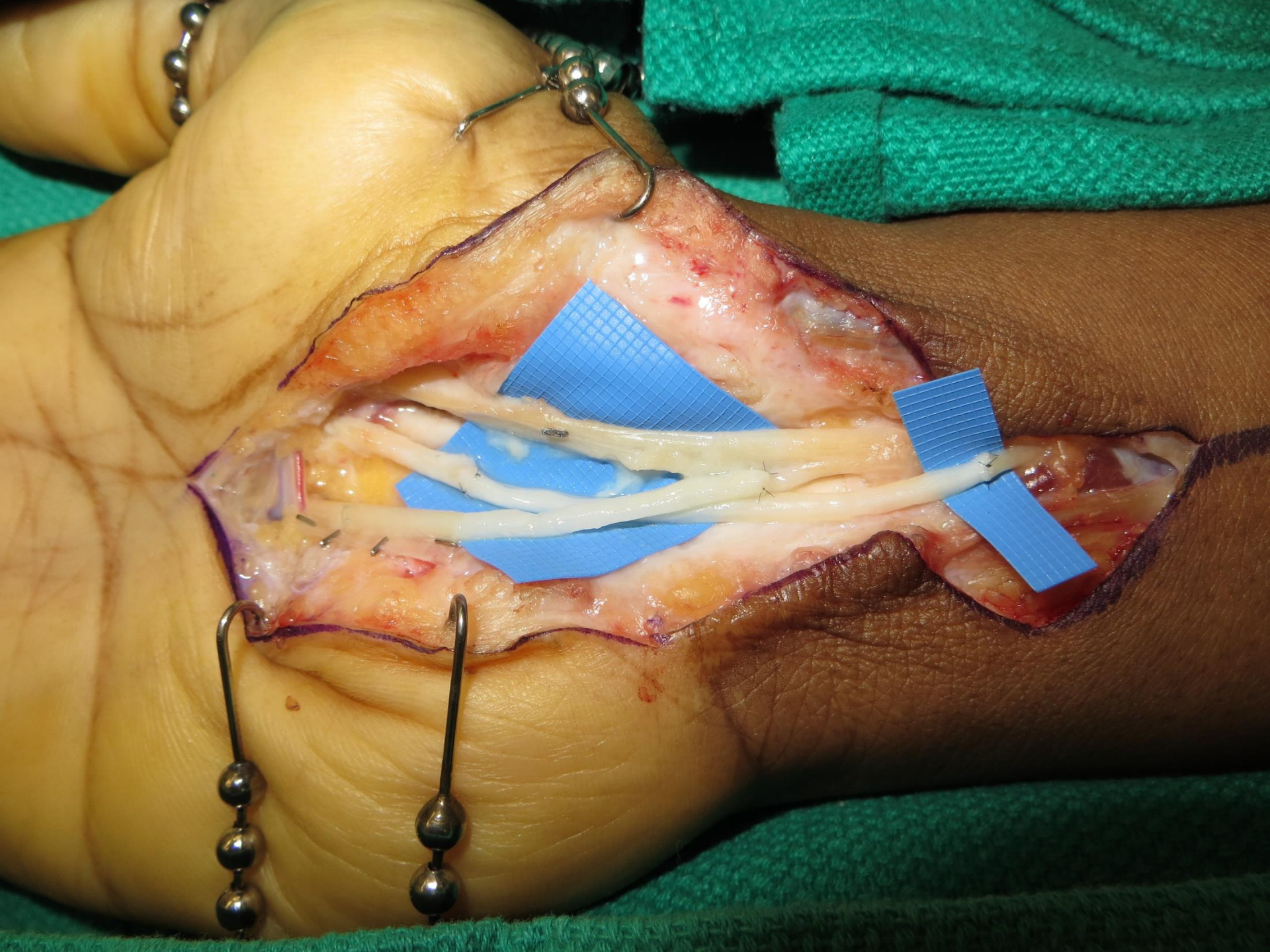
MEDIAN NERVE NEUROMA IATROGENIC INJURY



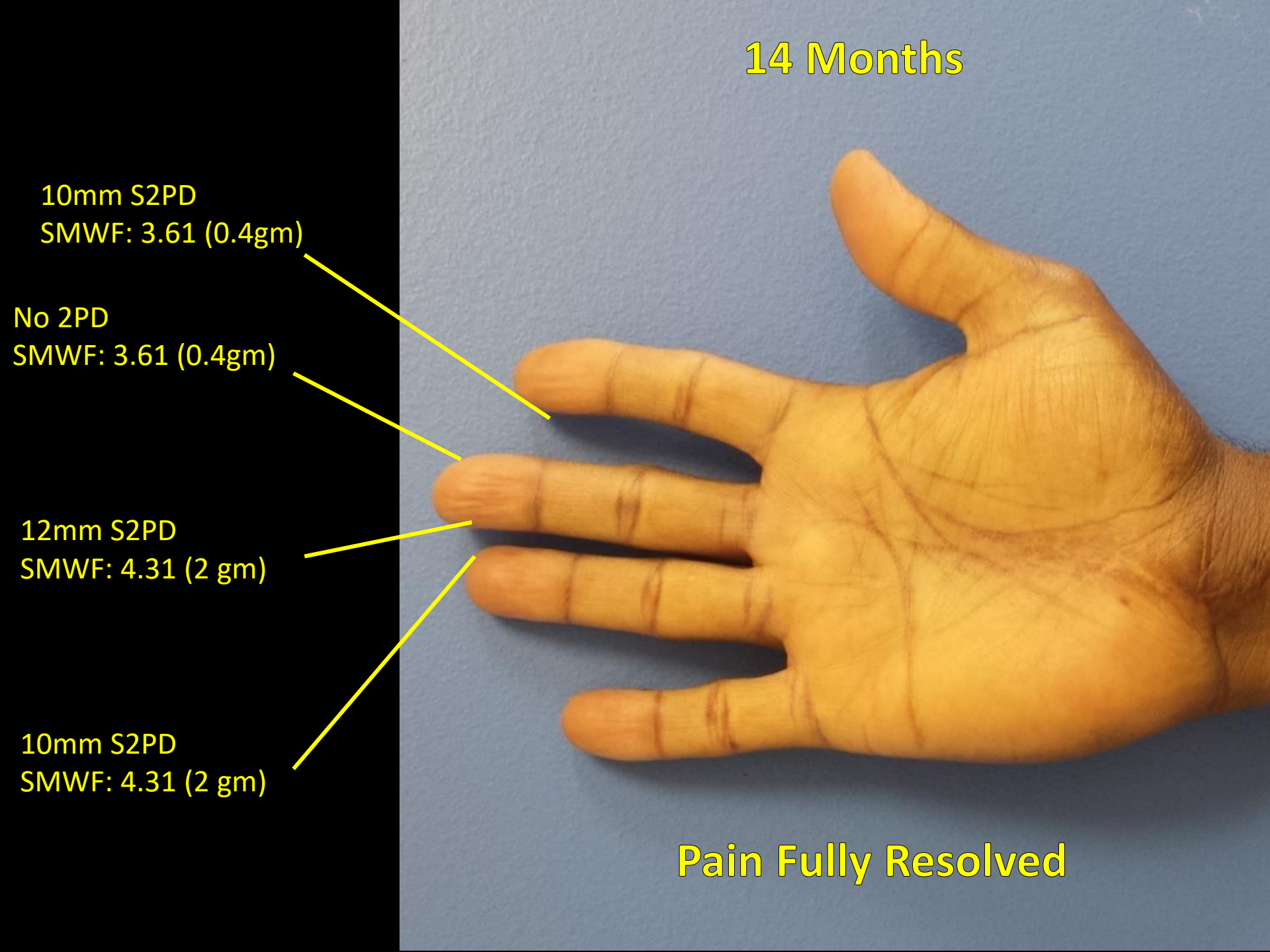

CM
INCHES
MEDLINE


MEDLINE
INCHES
CM
3cm
8cm


MEDLINE
INCHES
CM
5cm
5cm

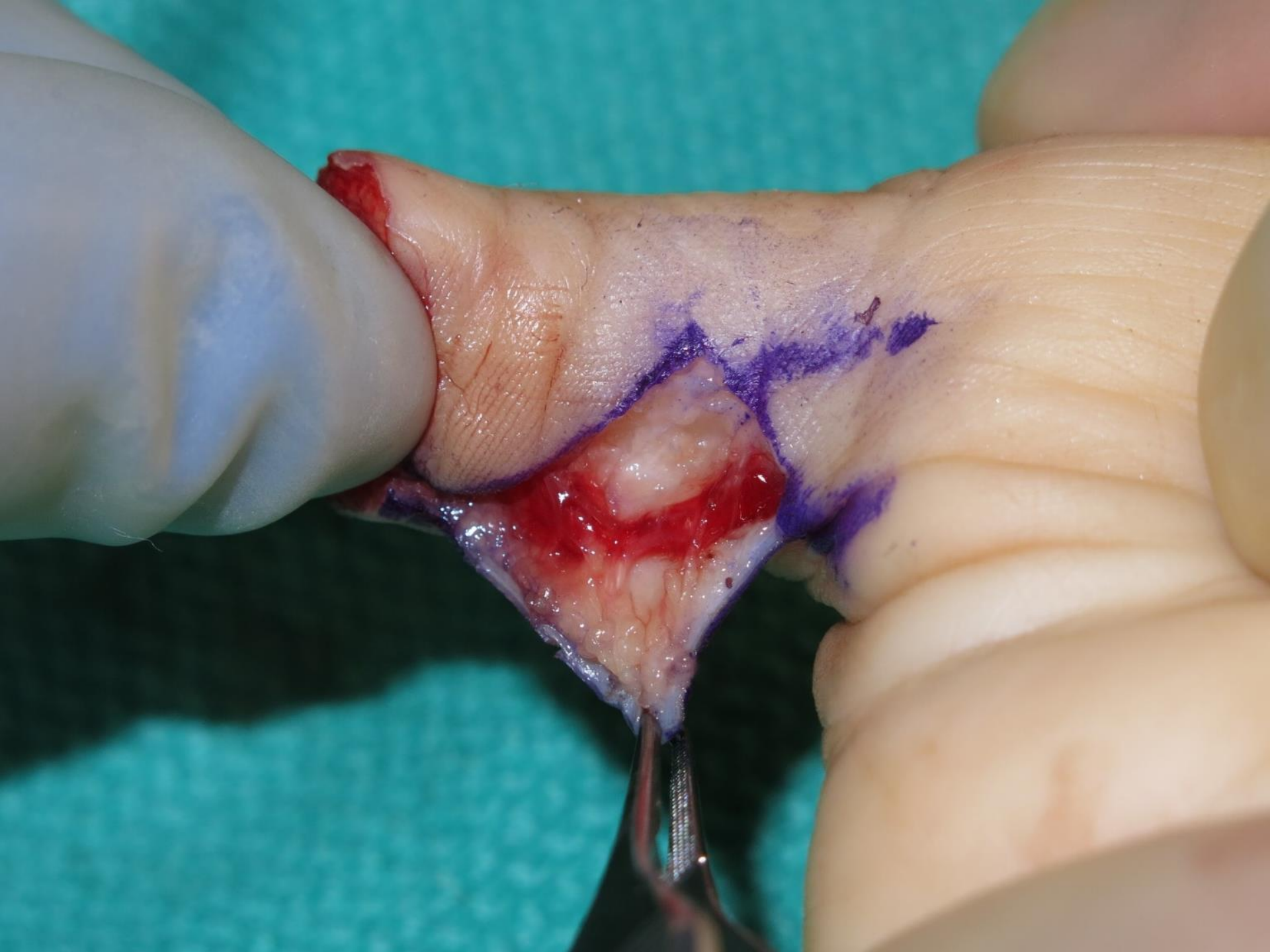


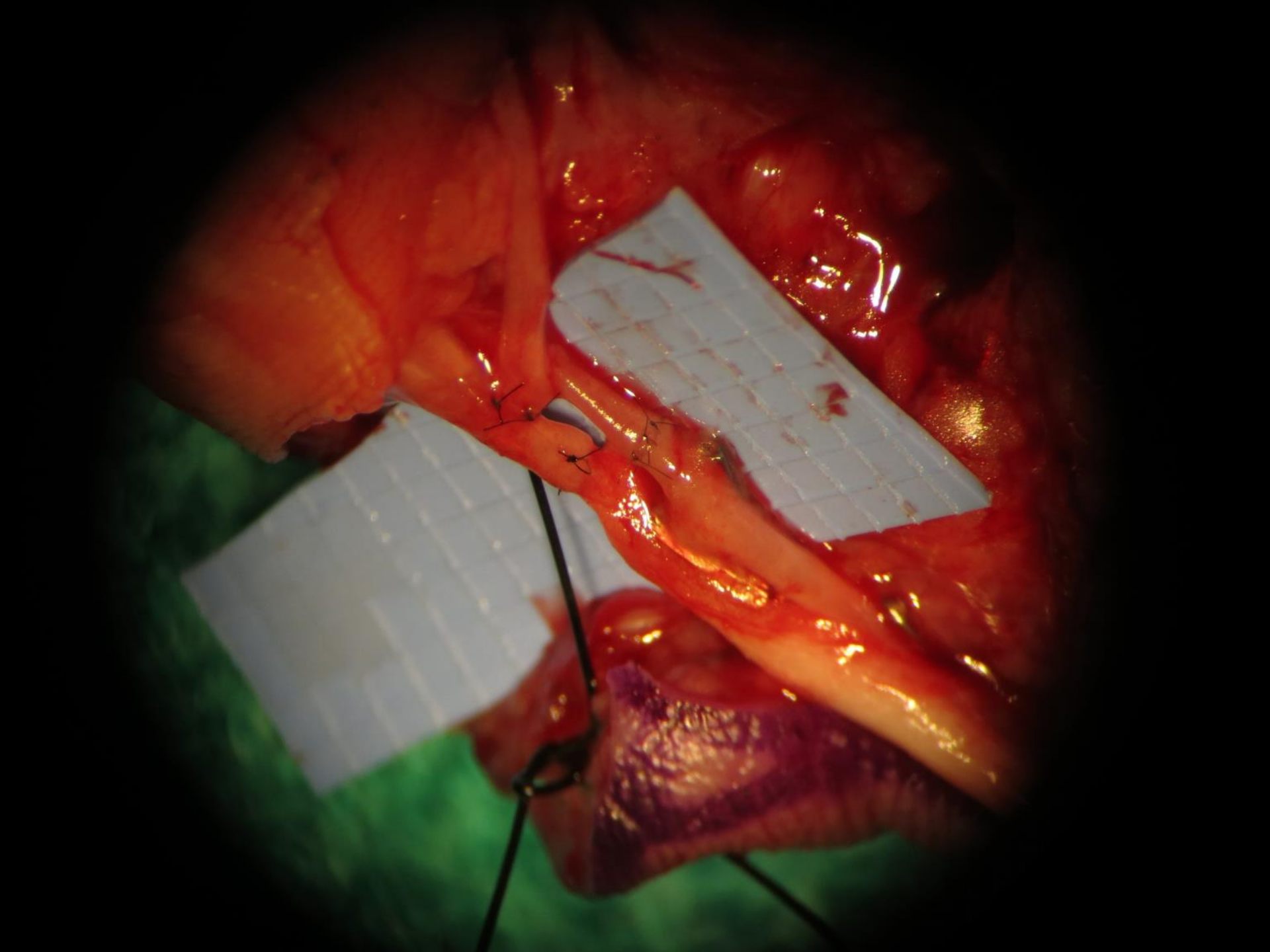

3
4
5
6
7
8
9
10

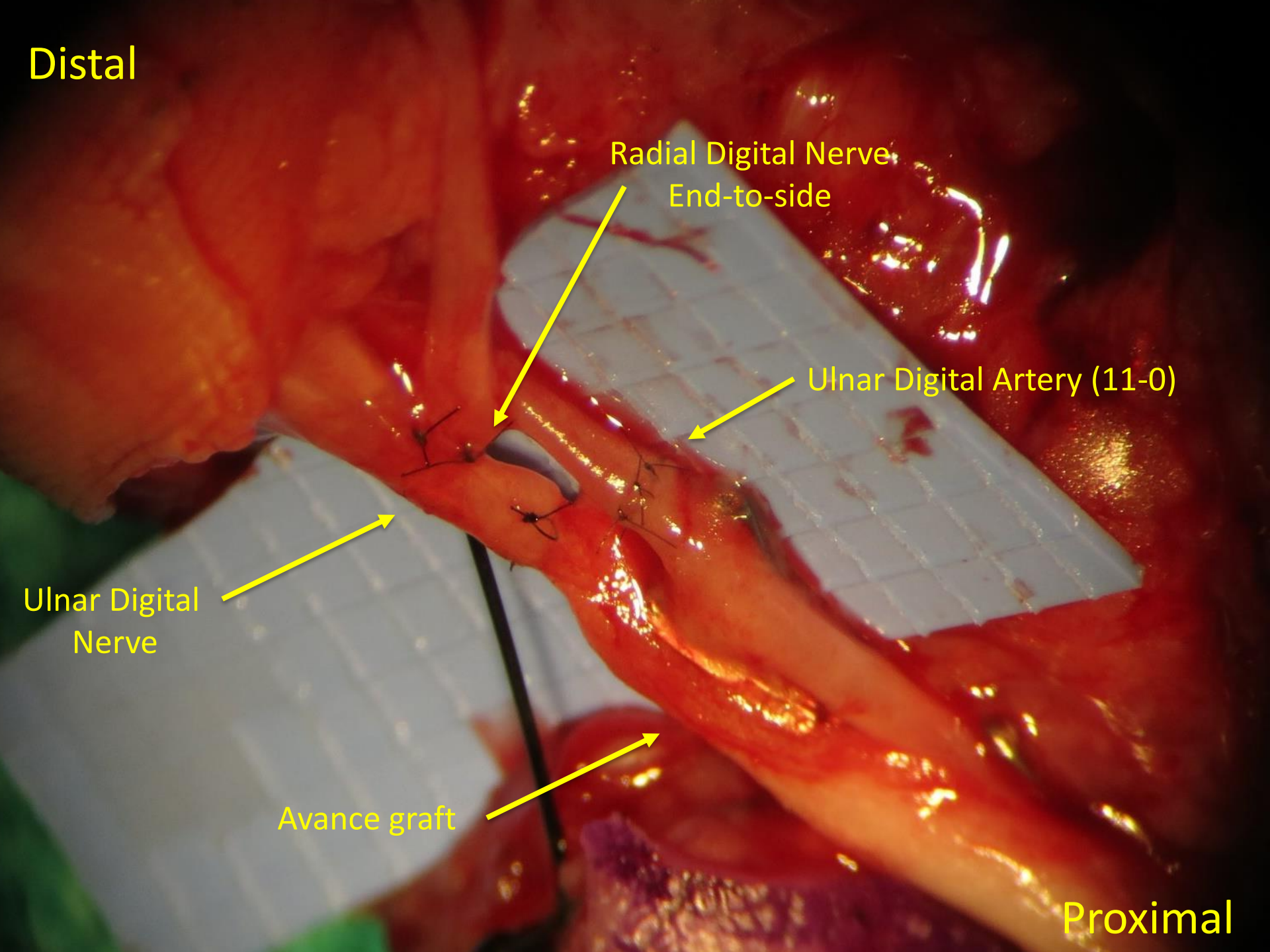

14 Months
10mm S2PD
SMWF: 3.61 (0.4gm)
No 2PD
SMWF: 3.61 (0.4gm)
12mm S2PD
SMWF: 4.31 (2 gm)
10mm S2PD
SMWF: 4.31 (2 gm)
Pain Fully Resolved

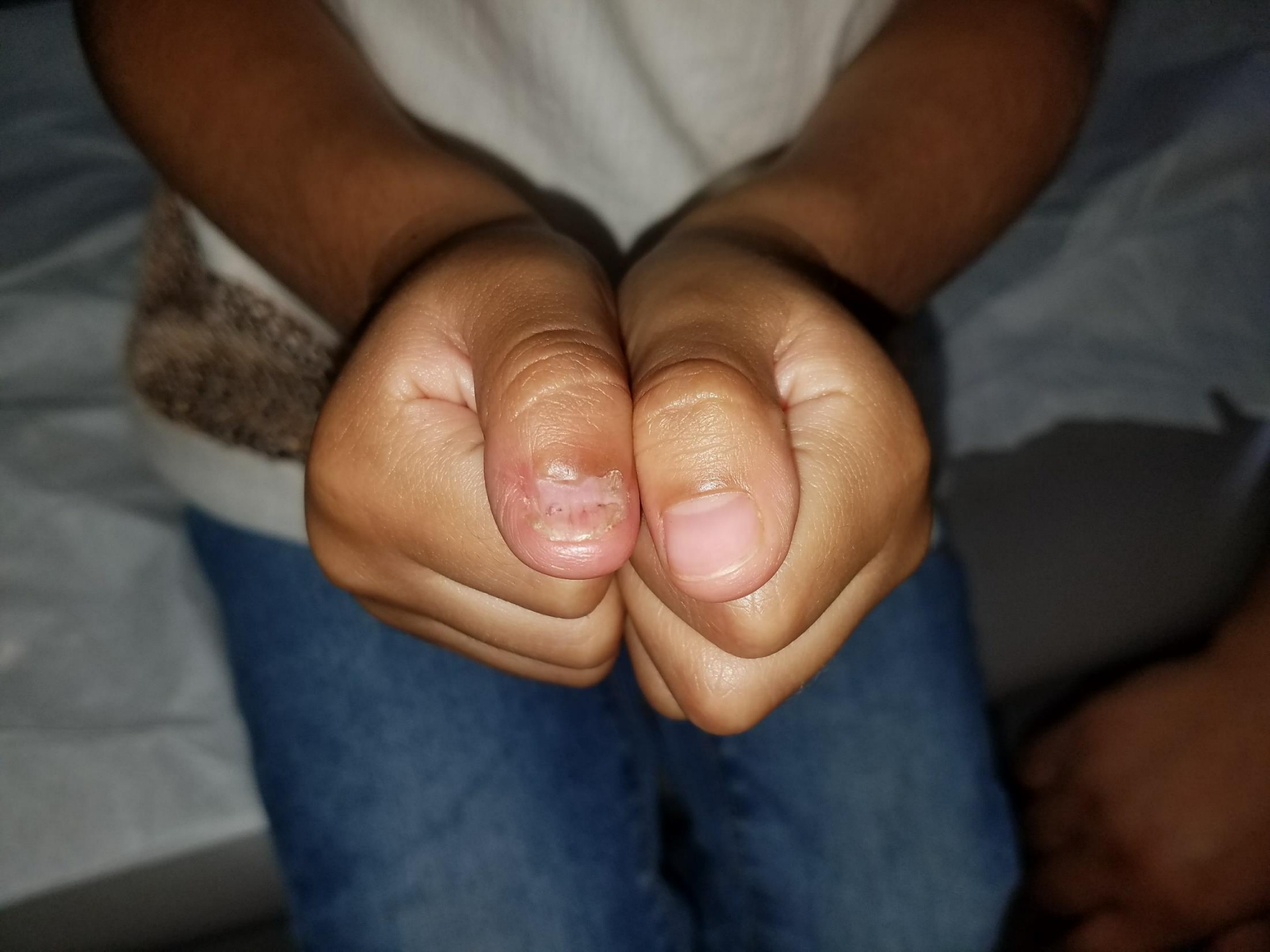
THUMB AVULSION AMPUTATION

2.5 year old girl

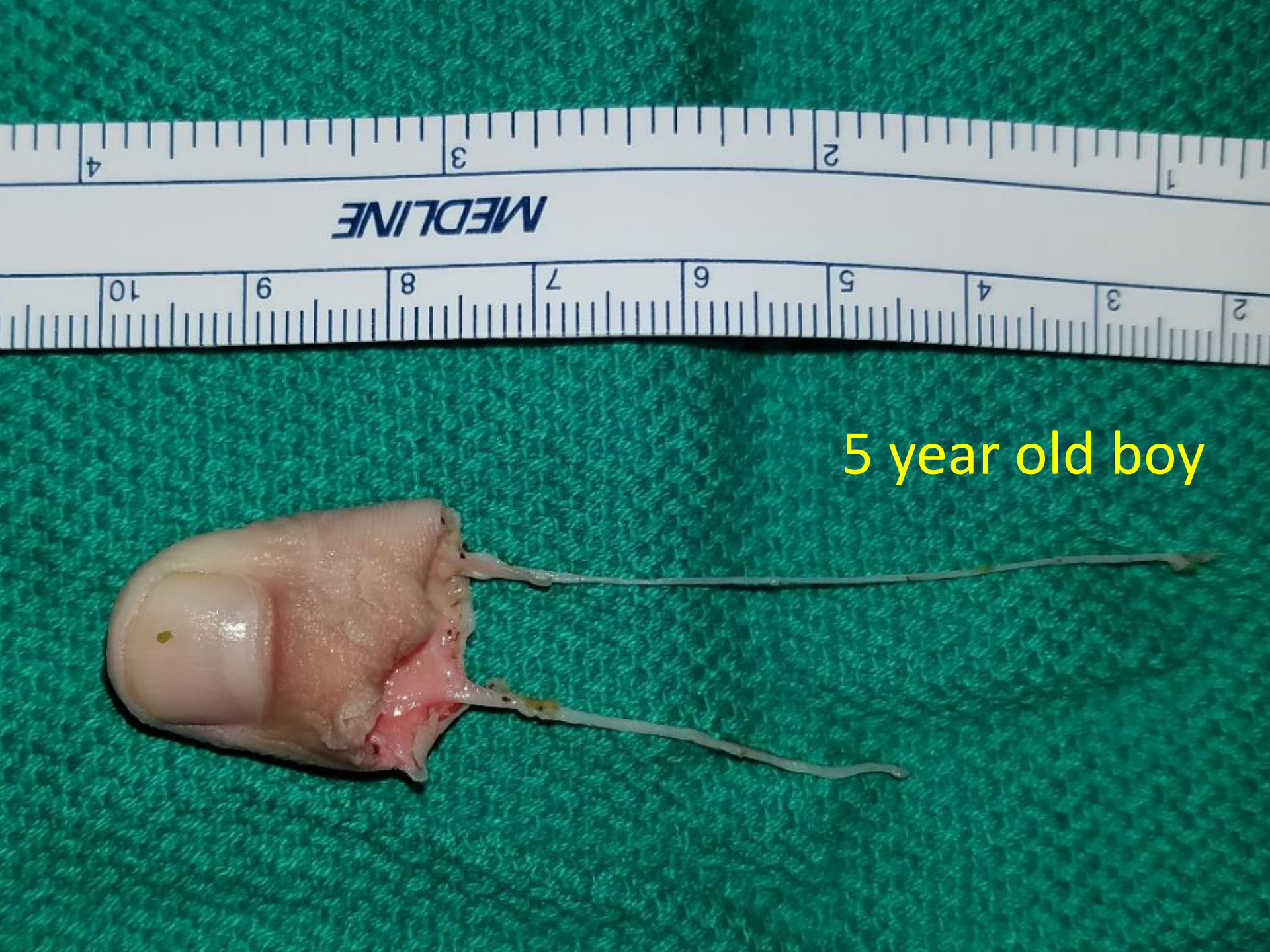




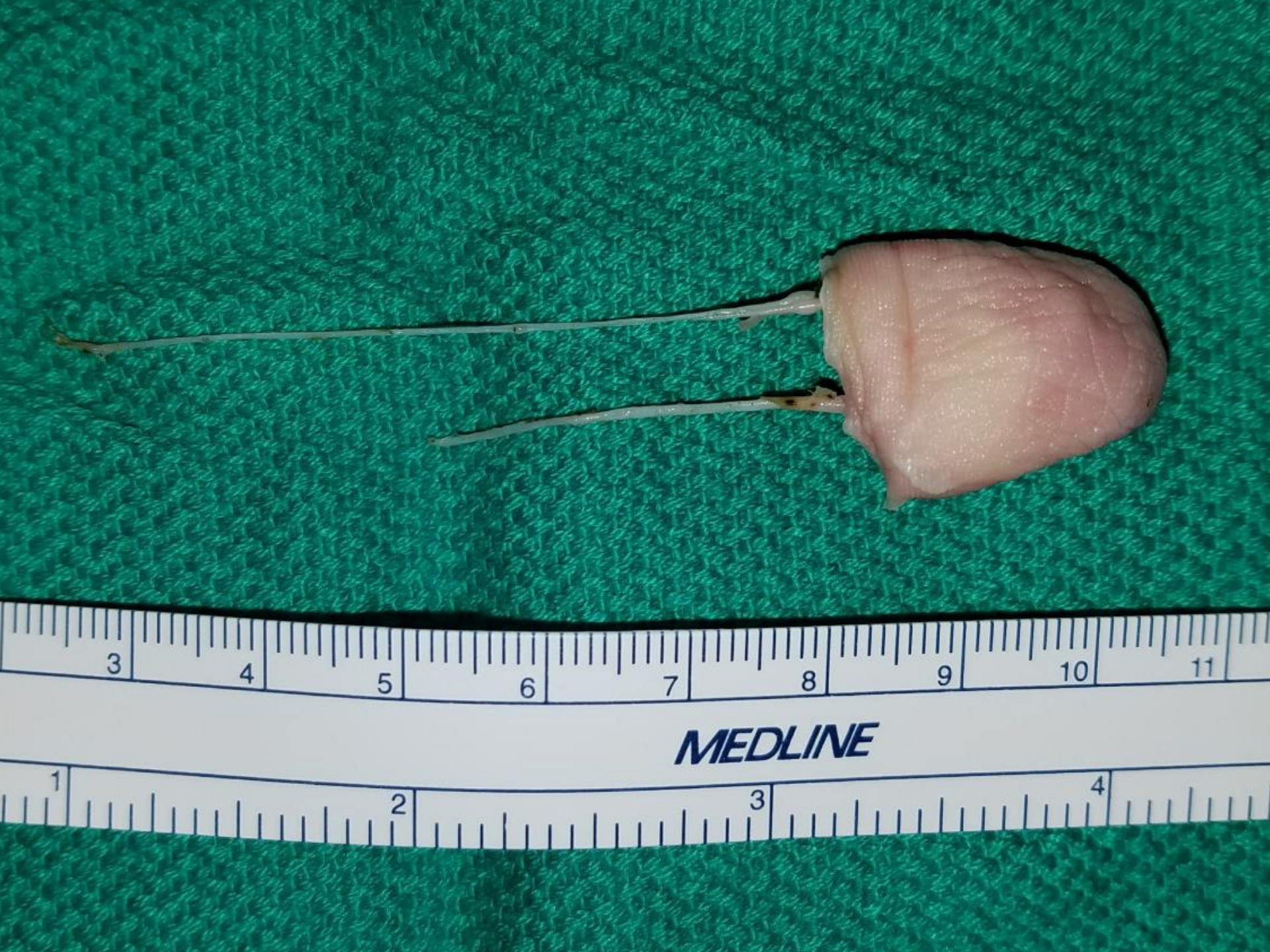

Distal
Radial Digital Nerve
End-to-side
Ulnar Digital Artery (11-0)
Ulnar Digital
Nerve
Avance graft
Proximal



THUMB AVULSION AMPUTATION HORSE BITE


MEDLINE
5 year old boy


MEDLINE

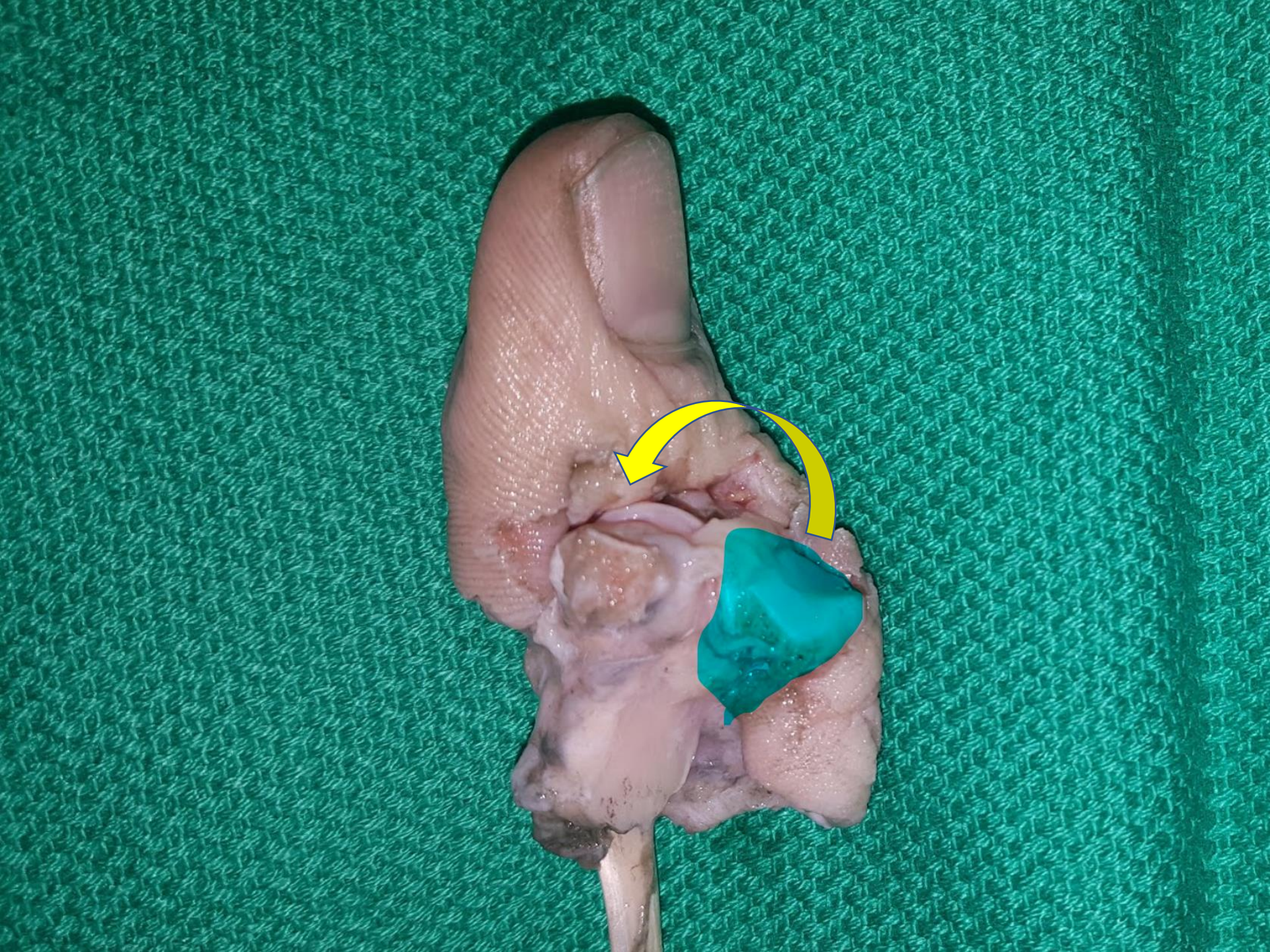

MEDLINE


3 weeks


4 months
Light touch

CEMENT MIXER VS. THUMB
35 YEAR OLD MAN


AG
Ex



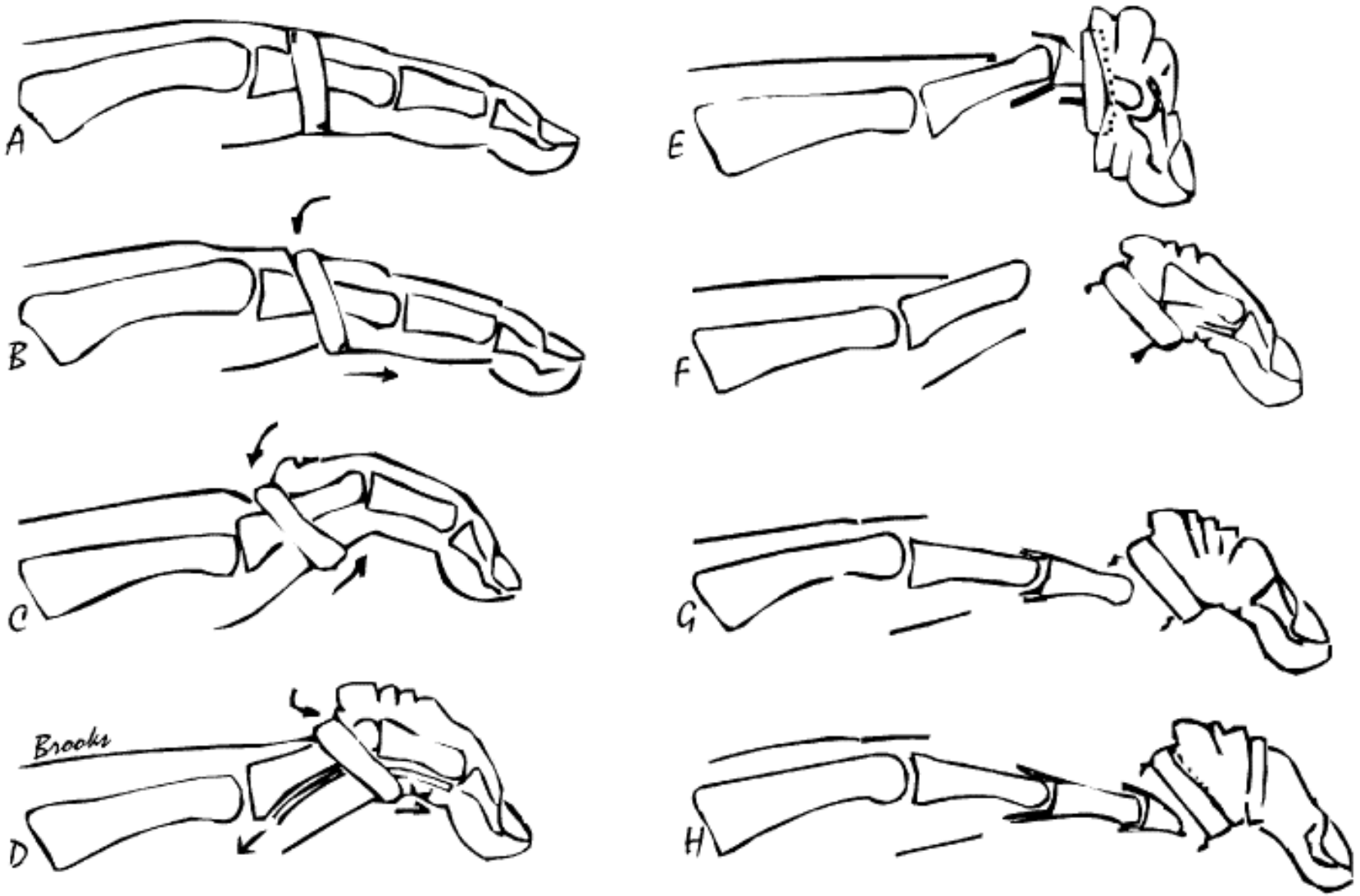
1576720] - Left hand

Full Field

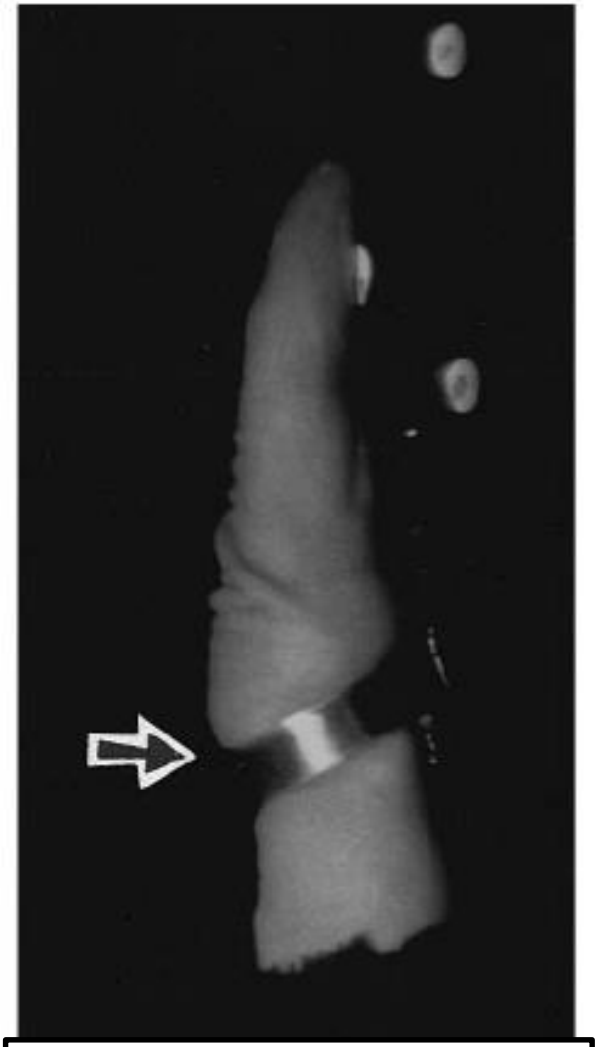
50 / 50

RING AVULSION INJURY

Mechanism of Ring Avulsions



Clin Plastic Surg 34 (2007) 187–195



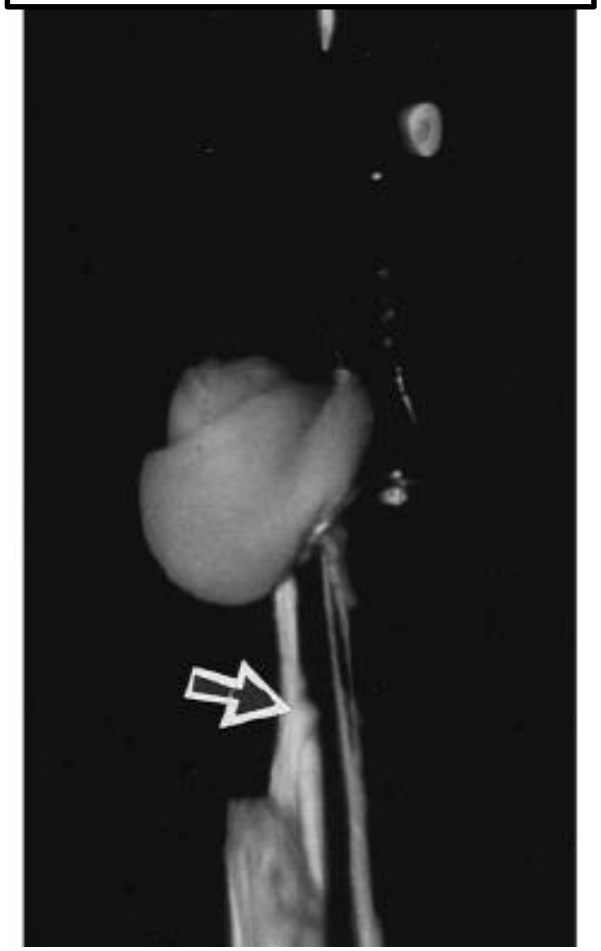
Ring migration and angulation
Skin compression and distal translation

Transverse skin rupture
Ring plows distally, deep to subq tissue

Rupture of the remaining skin (arrow)

Initial rupture of neurovascular bundle (arrow)
Flexor still intact

Progressive disruption of flexor;
Near complete NVB rupture



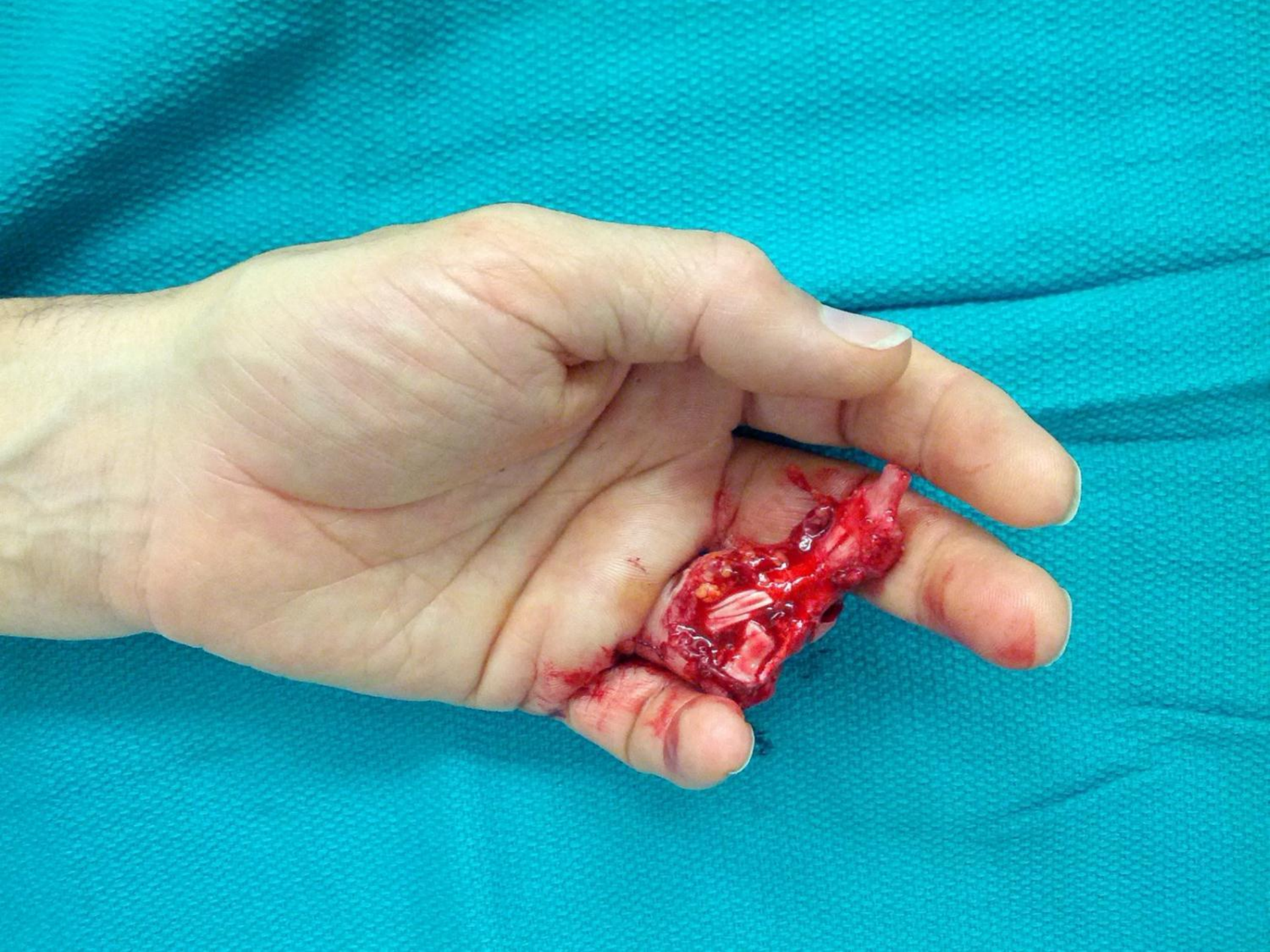
Flexor tendon rupture and elastic recoil

J Hand Surg 1999;24A:1249–1253

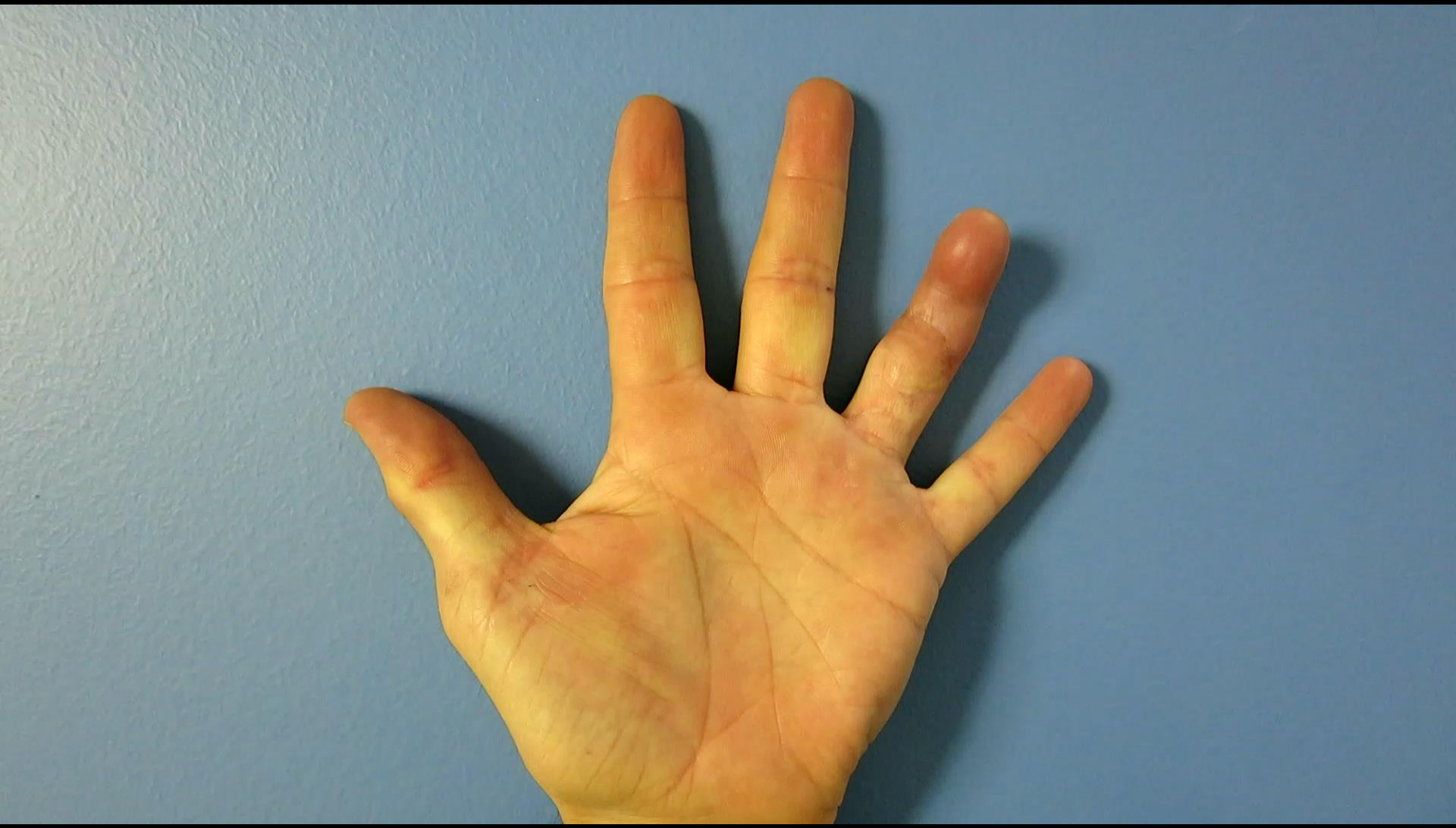
RING AVULSION INJURY

Concept

- If there is a gap in
  - Soft tissues
  - Artery
  - Vein
  - Etc…
- There will be a gap in the nerve
- Strategy:
  - Bridge all gaps aggressively
  - Soft tissues
  - Vessels
  - Nerves




RDN: 10 S2PD
UDN: No 2PD
SWMF: 3.61 (0.4mg) for both
UDN and RDN

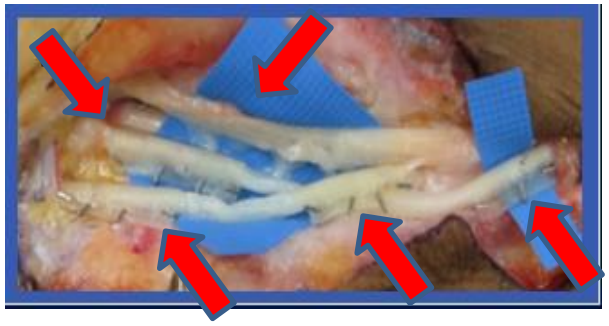


RING AVULSION INJURY


Slide

Do Nerve Protectors Affect Recovery?

- Zoldos et al. 2017 AAHS ePoster 169.
- Subgroup analysis of upper extremity nerve repairs from the RANGER Registry
- All repairs performed with peripheral nerve allograft
- Trend toward higher meaningful recovery with Protectors (89%) vs Control (79%)



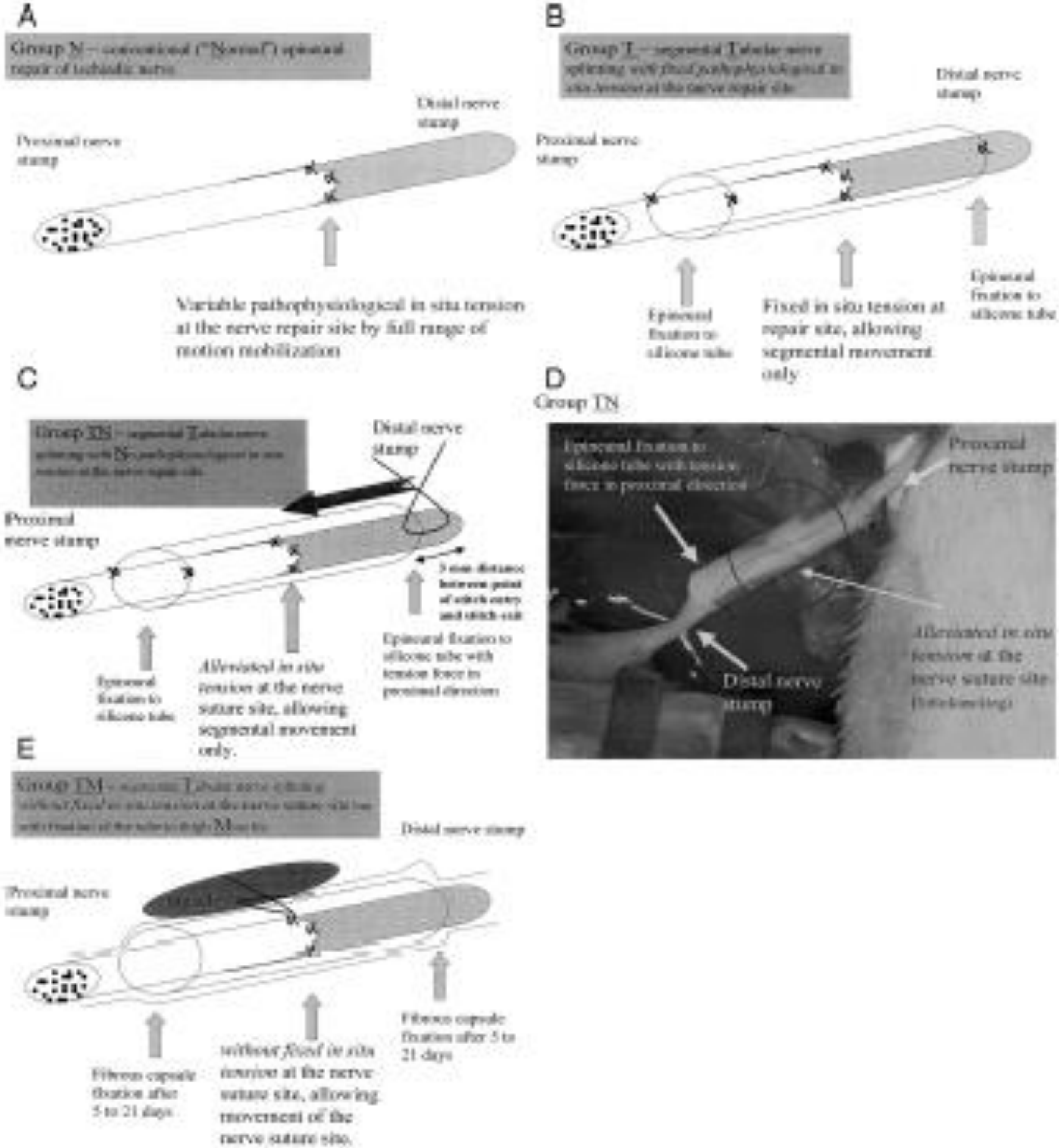
Factor	PNA w/Protector	PNA only
Age (years)	43±15	43±20
No. Repairs	19	27
Follow-up (days)	361±188	409±201
Gap Length (mm)	33±14	29±11
Time to Repair		
Acute (< 3 weeks)	9	18
Delayed (3 weeks-3 mths)	5	1
Chronic (> 3 months)	5	8
Type of Nerve		
Sensory	3	5
Mixed	12	17
Motor	4	5
Mechanism of Injury		
Laceration	7	16
Complex	12	11
Meaningful Recovery	**89%***	**79%***

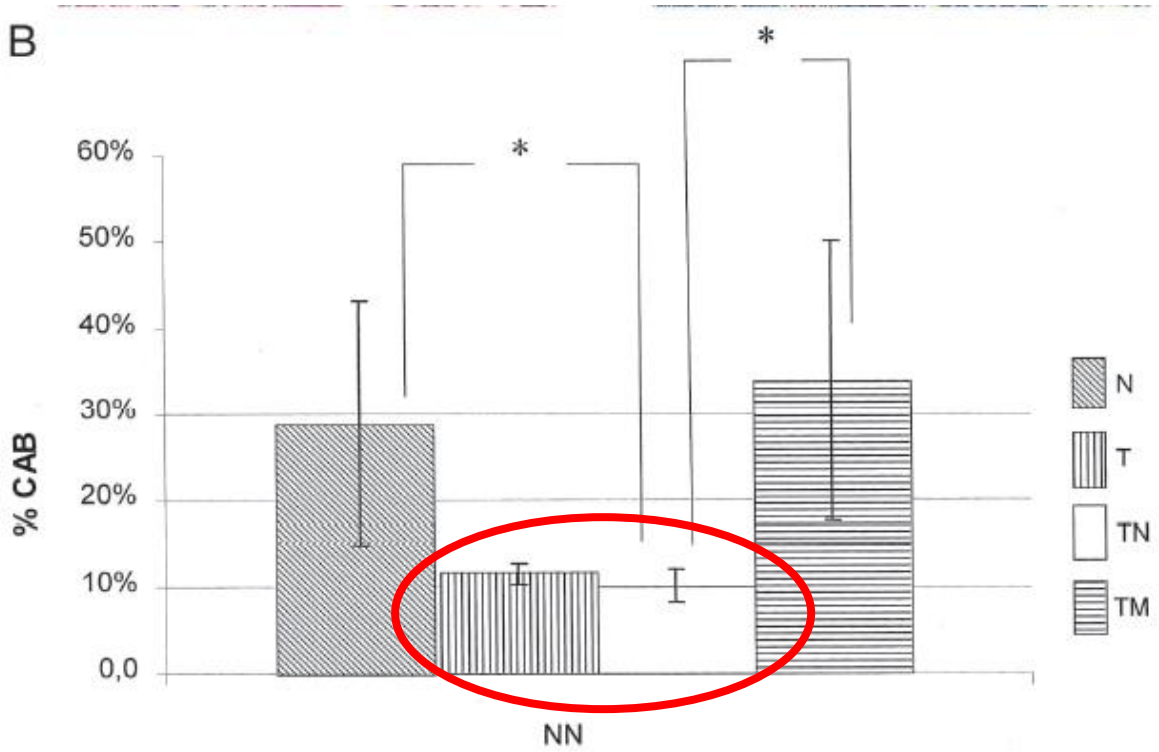
*p=0.26, Fisher's exact test
Age, follow-up days and gap length are presented as Mean±SD

The Journal of TRAUMA® *Injury, Infection, and Critical Care*

Alleviated Tension at the Repair Site Enhances Functional Regeneration: The Effect of Full Range of Motion Mobilization on the Regeneration of Peripheral Nerves—Histologic, Electrophysiologic, and Functional Results in a Rat Model

Robert Schmidhammer, MD, Shahin Zandieh, Rudolf Hopf, Ingrid Mizner, Linda E. Pelinka, MD, Albert Kroepfl, MD, and Heinz Redl, PhD


A
B
Variable pathophysiological in situ tension at the nerve repair site by full range of motion mobilization
Fixed in situ tension at repair site, allowing segmental movement only
C
D
Group TN
Distal nerve stump
Proximal nerve stump
Proximal nerve stump
Distal nerve stump
Alleviated in situ tension at the nerve suture site, allowing segmental movement only.
E
Distal nerve stump
Proximal nerve stump
without fixed in situ tension at the nerve suture site, allowing movement of the nerve suture site.



Suture Alone

with Tension Relief Tube 1

with Tension Relief Tube 2

Tube without Tension Relief

Other Reasons to Use Connector or Wrap

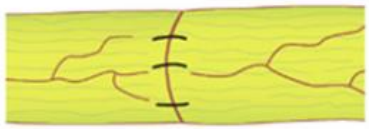
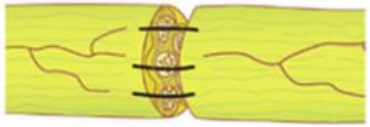
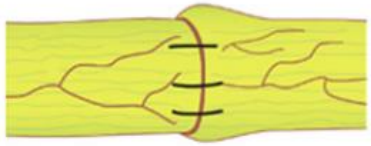
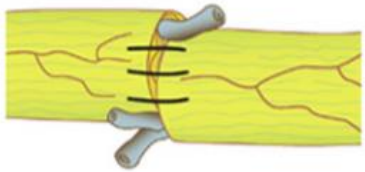
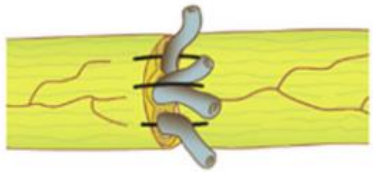
- “De-tensioning” the coaptation site
- Leveling the playing field in nerve coaptation

SCIENTIFIC ARTICLE

Technical Assessment of Connector-Assisted Nerve Repair

Jonathan Isaacs, MD,* Bauback Safa, MD,† Peter J. Evans, MD, PhD,‡ Jeffrey Greenberg, MD§

J Hand Surg Am, 2016

Grade	Description	Example Image
Excellent	End-to-end alignment, no gapping, adequate tension and approximation, no fascicle extrusion	
Good	End-to-end alignment gapping < 1 mm, no fascicle extrusion Or End-to-end alignment, excessive approximation, no fascicle extrusion	 
Fair	End-to-end alignment gapping > 1 mm, fascicle extrusion	
Poor	Inadequate alignment regardless of tension, fascicle extrusion	

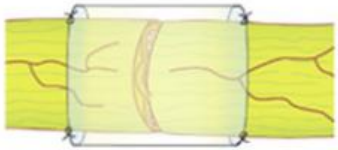
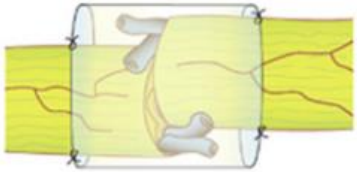
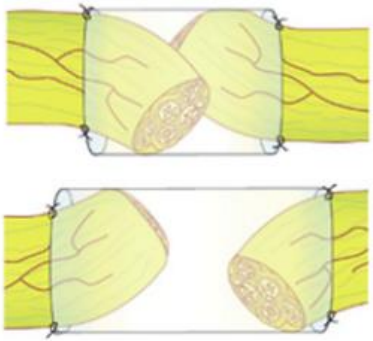
Grade	Description	Example Image
Excellent	End-to-end alignment with no gapping	
Good	End-to-end alignment with some gapping ≤ 2 mm	
Fair	Partial alignment with some overlap between ends and some fascicles not approximated	
Poor	Inadequate alignment of both stumps within the connector gap is > 5 mm, stump is pushed against the connector wall or stumps overlap	

FIGURE 3: Example of a poorly aligned nerve repair utilizing the connector-only technique.

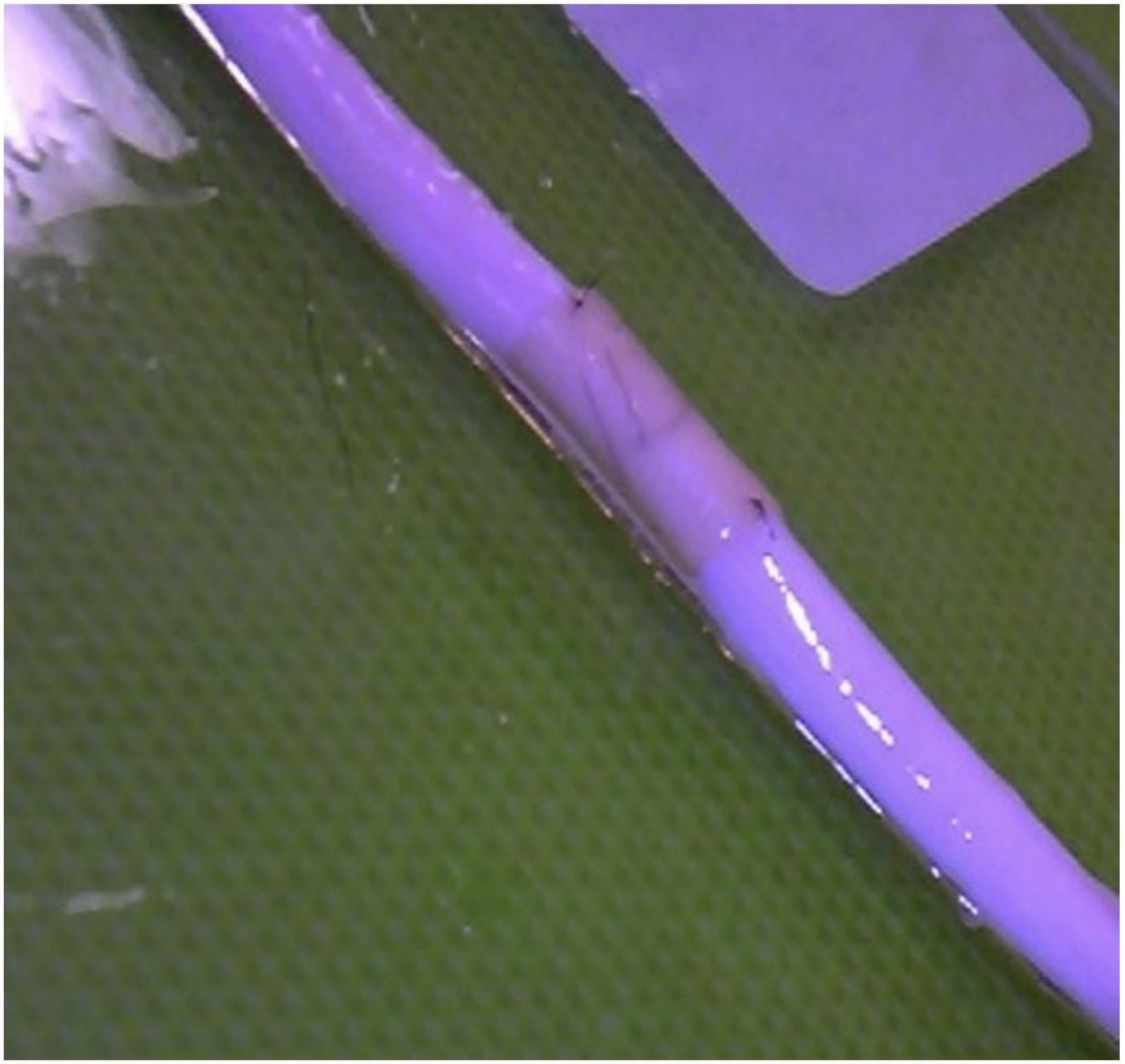


FIGURE 4: Example of a well-aligned nerve repair utilizing the connector-assist technique. Note the aligning sutures seen through the connector. The walls of the connector mold and direct the nerve ends into proper alignment.

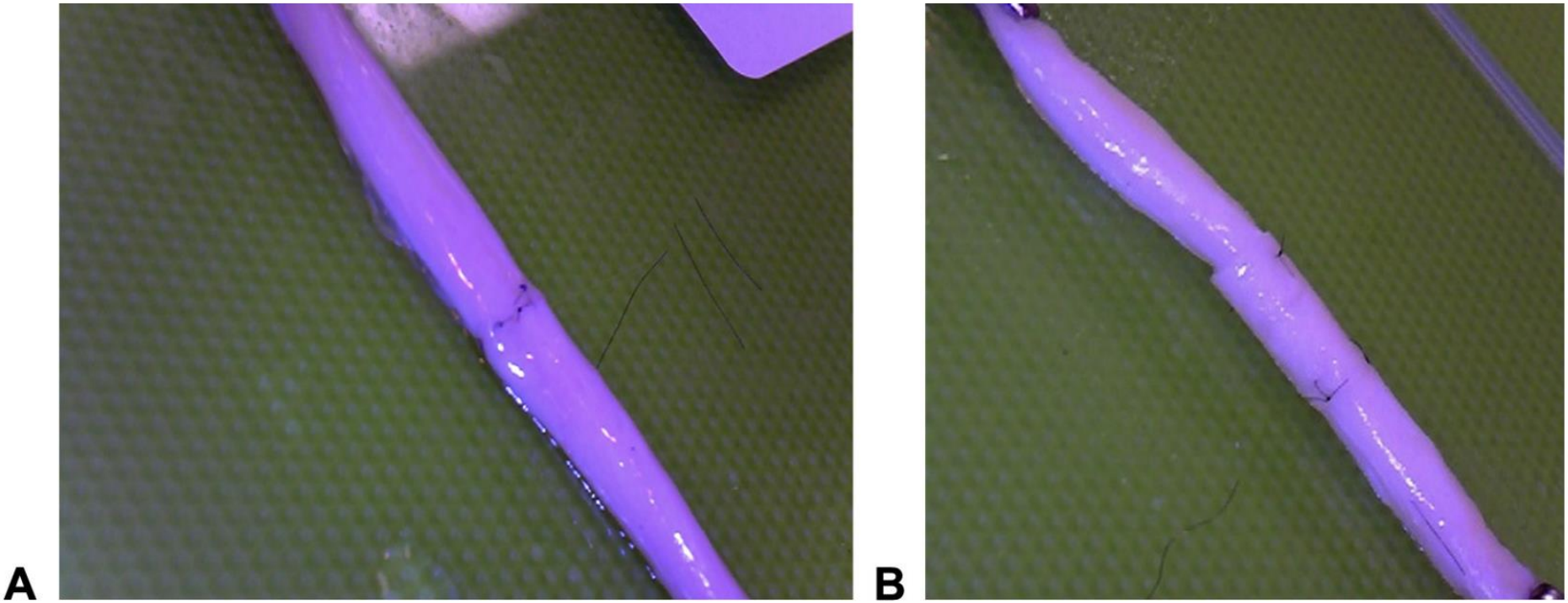


FIGURE 5: Examples of well aligned repairs. **A** Suture-only technique. **B** Connector-only technique.

FIGURE 6: Example of an overtightened suture-only repair. Although the nerve ends are in gross alignment, note the fascicles pooching out the sides of the repair.

TABLE 1. Technical Scores of Cadaveric Nerve Repairs

Type	P	F	G	E
Connector-assisted experienced	1	1	2	11
Connector-assisted inexperienced	3	2	1	9
Connector-only experienced	1	3	6	5
Connector-only inexperienced	8	5	2	0
Suture-only experienced	0	4	2	9
Suture-only inexperienced	2	6	3	4

E, Excellent; F, Fair; G, Good; P, Poor.

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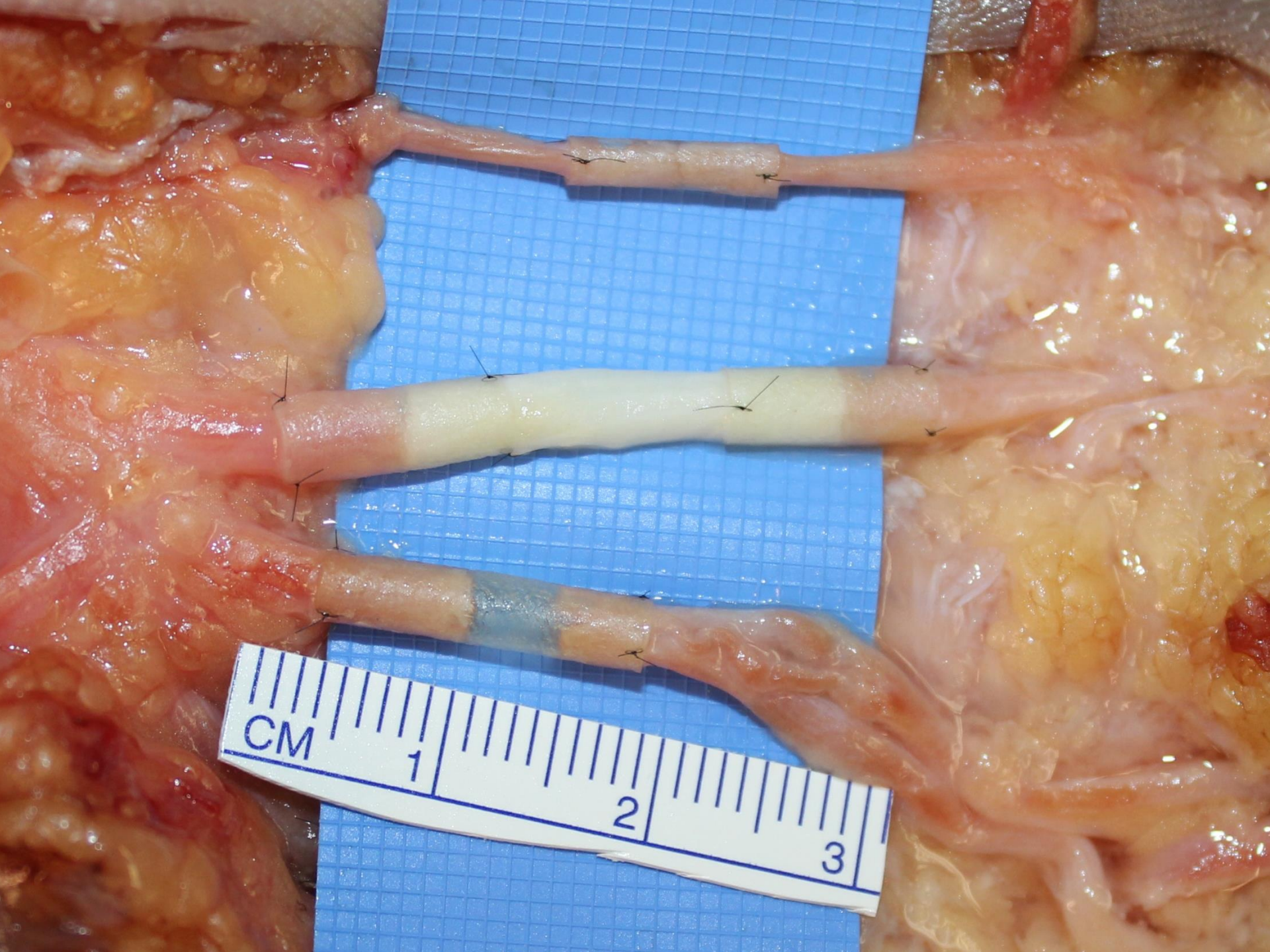
Connector-only experienced	1	3	6	5
Connector-only inexperienced	8	5	2	0
Suture-only experienced	0	4	2	9
Suture-only inexperienced	2	6	3	4

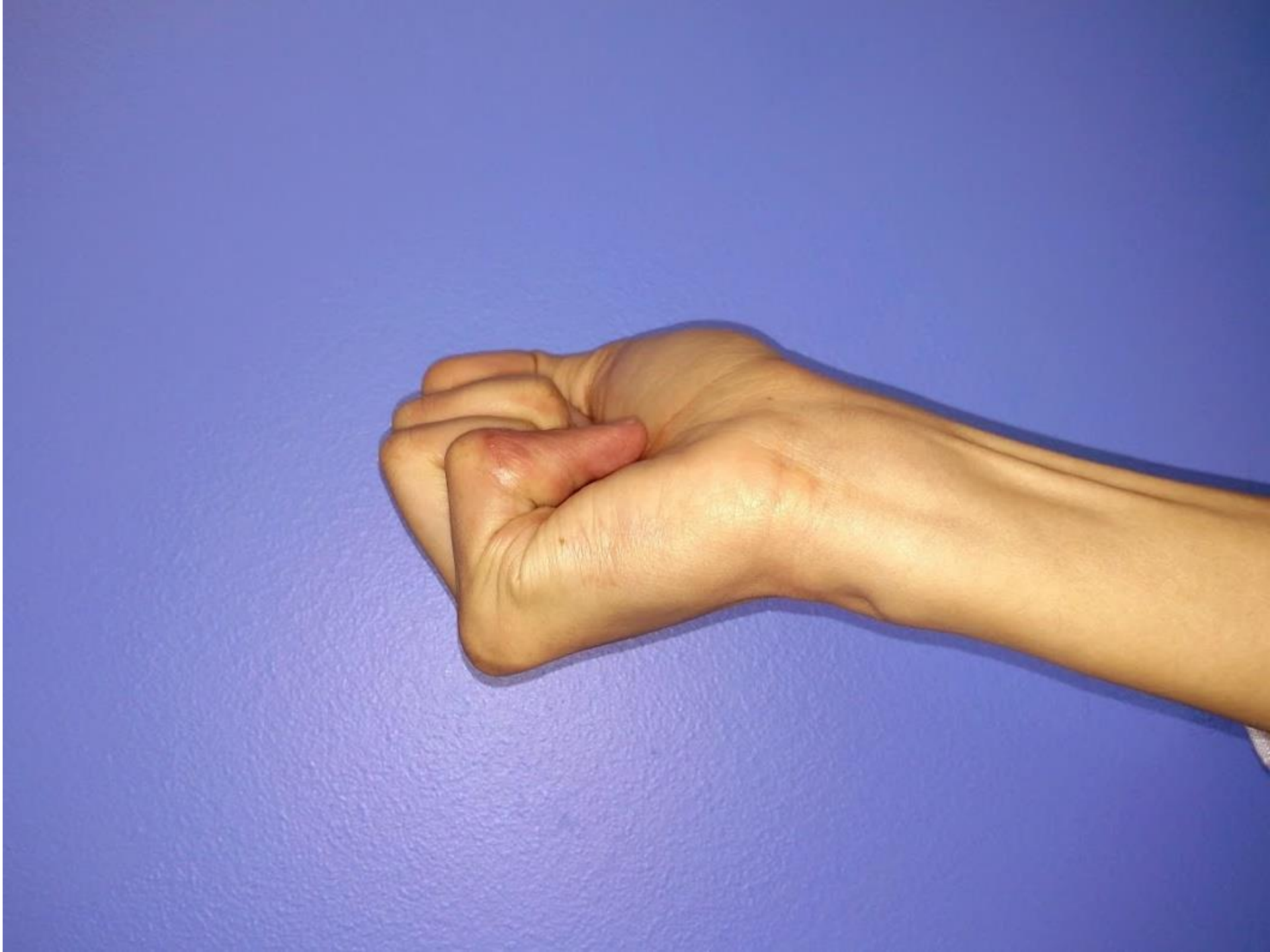
E, Excellent; F, Fair; G, Good; P, Poor.

Conclusions of the Study

- Inexperienced surgeons were more likely to achieve inadequate alignment with suture-only or conduit-only repairs.
- There was no significant difference in the technical alignment of conduit-assisted repairs between experienced and inexperienced surgeons


CM
1
2
3

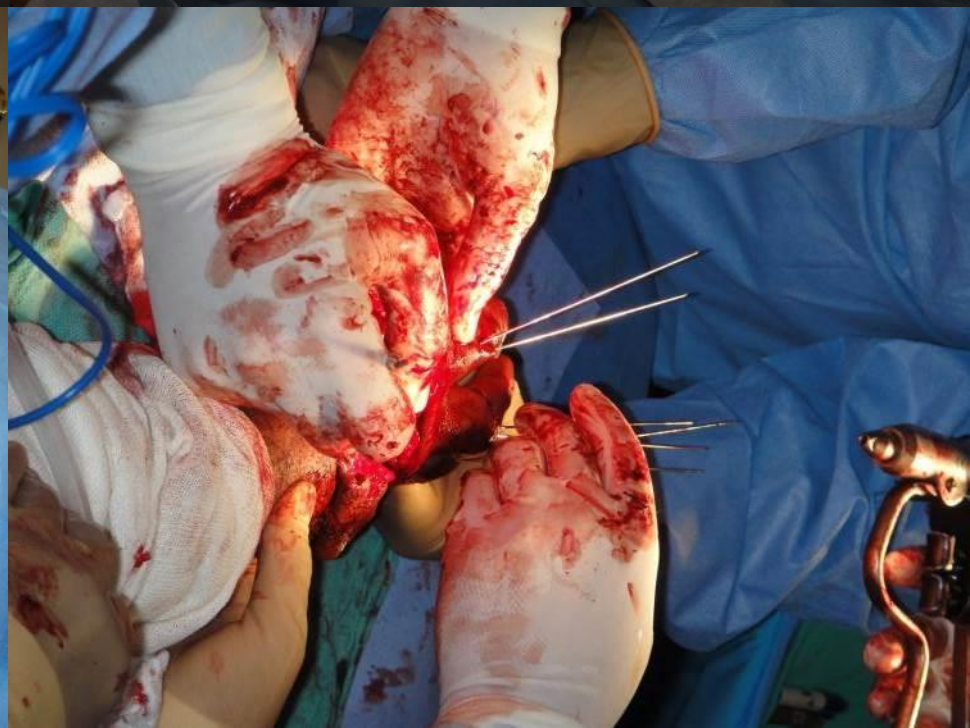

UDN: 10 S2PD
RDN: 7mm M2PD
SWMF: 3.61 (0.4mg) for both UDN and RDN

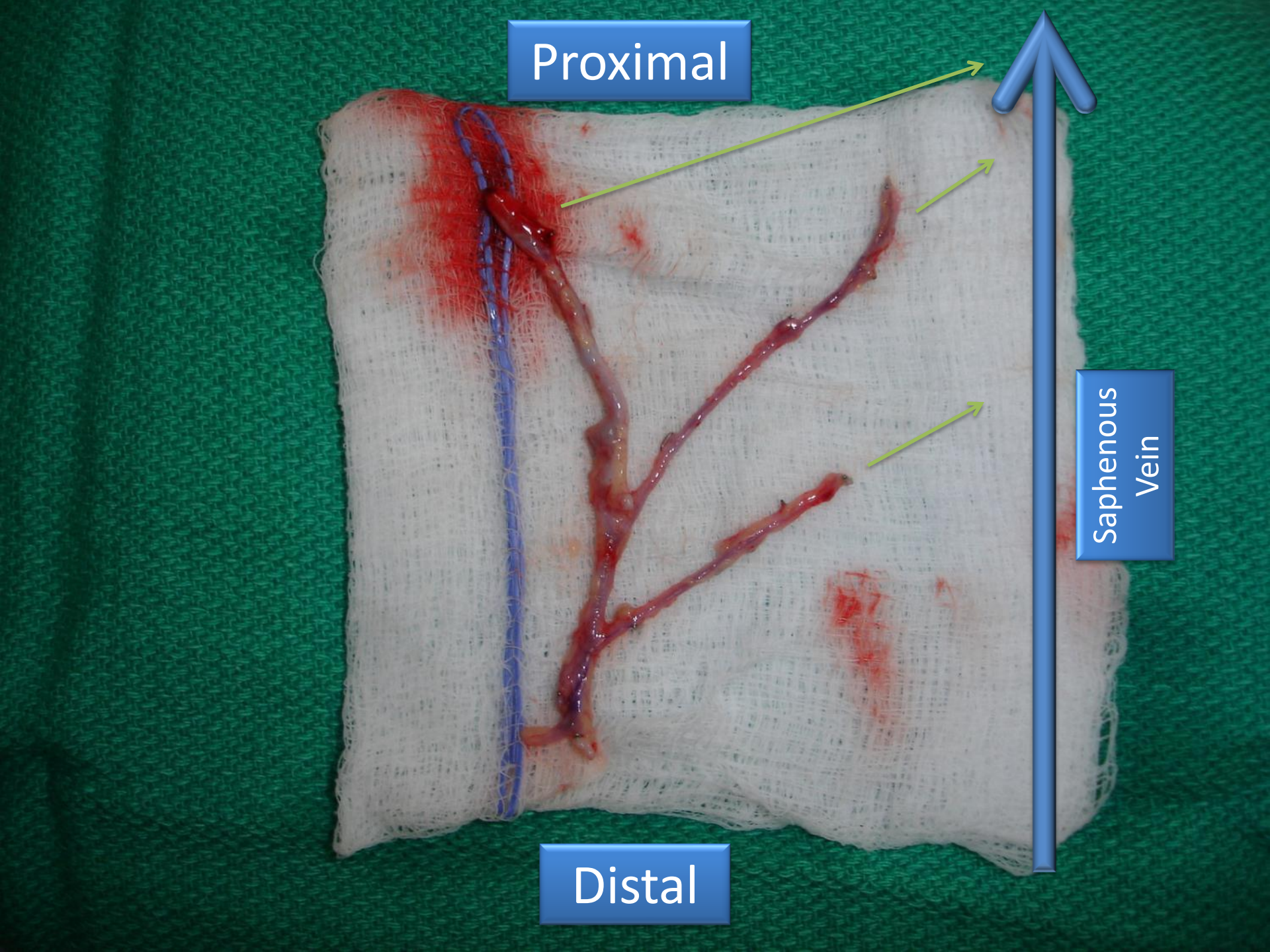


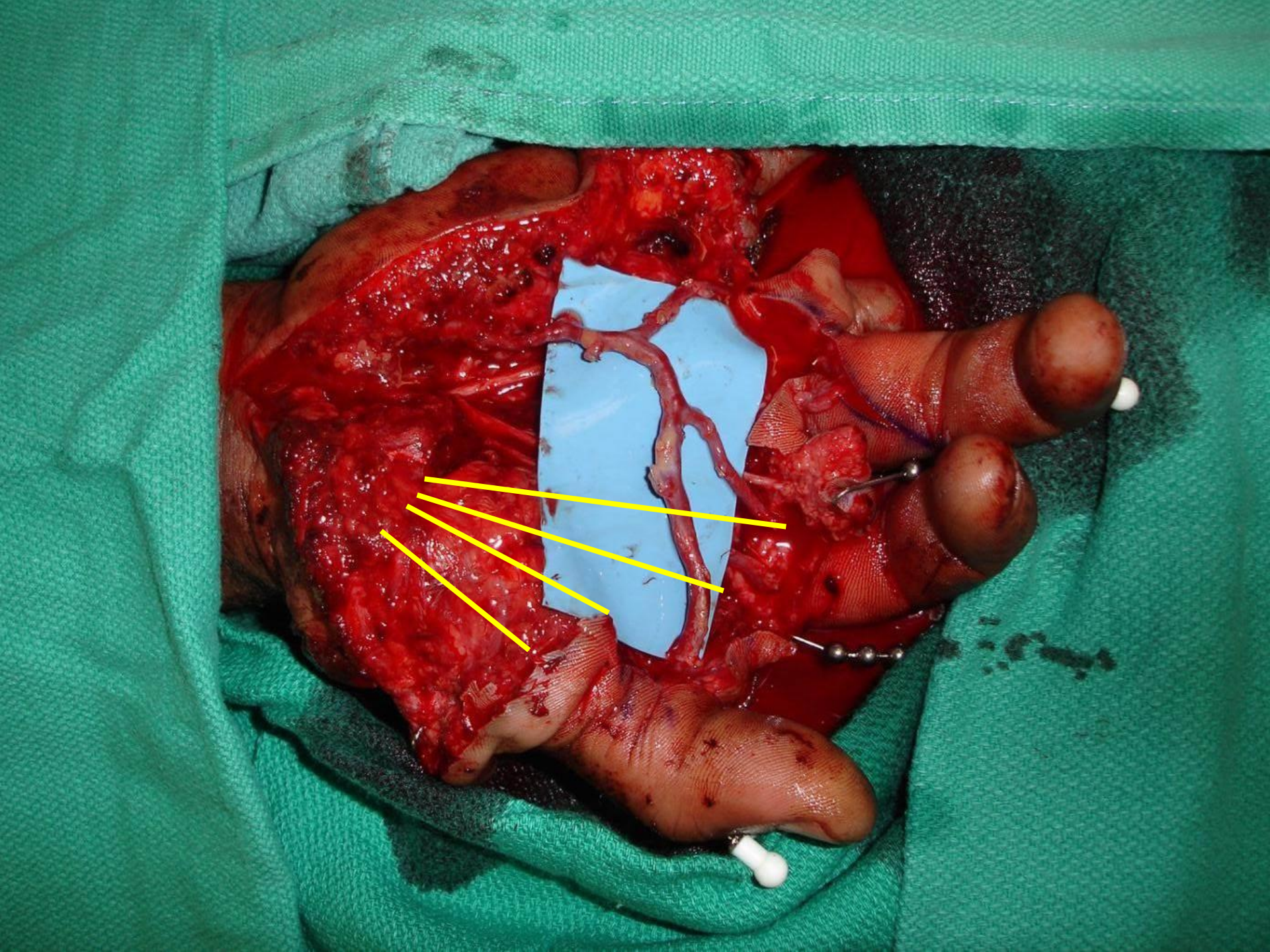
MULTI-LEVEL MUTILATING INJURY

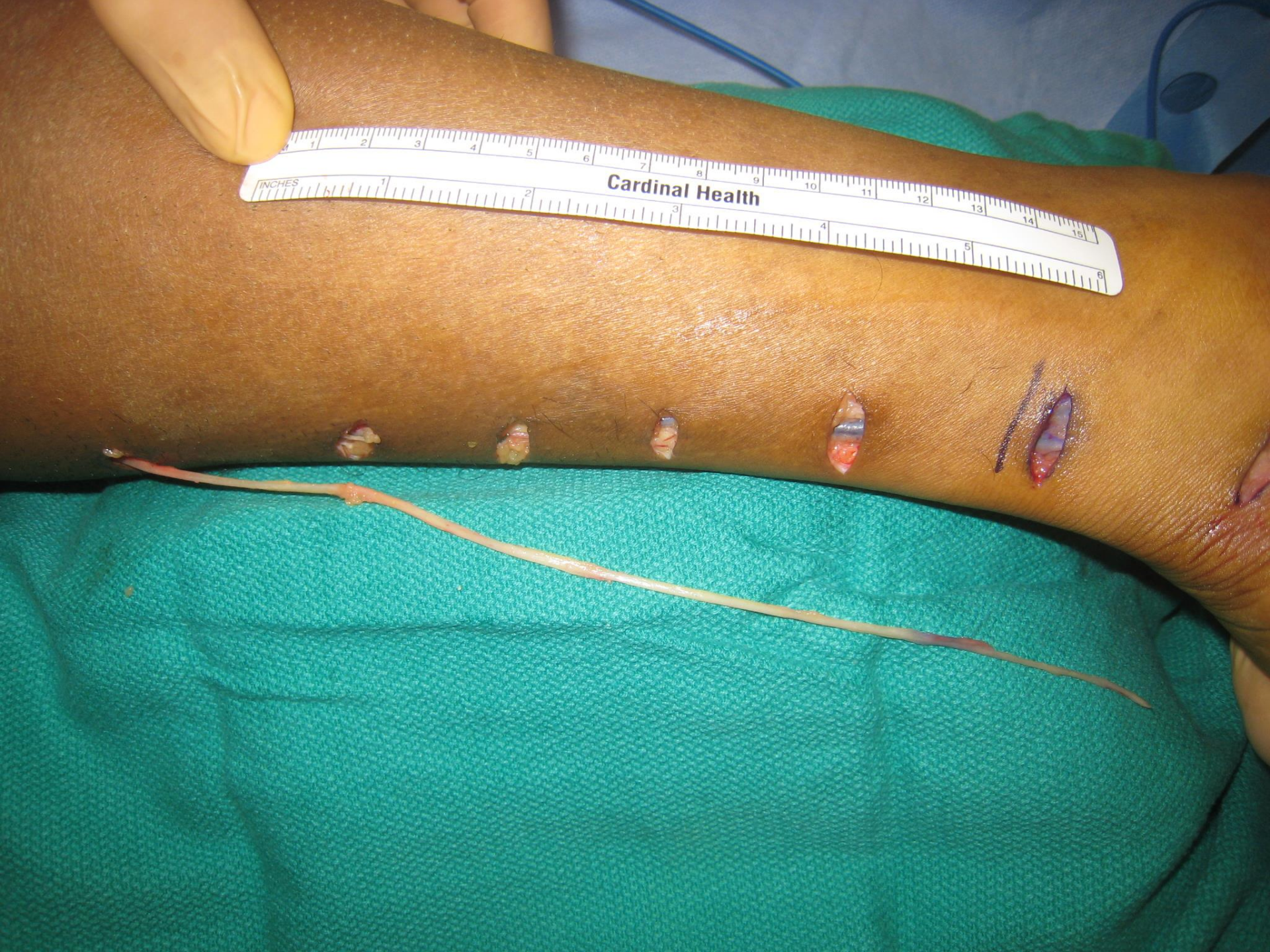

CENTER
04.19.1973
[08:52]
RT-01
EMR1025629

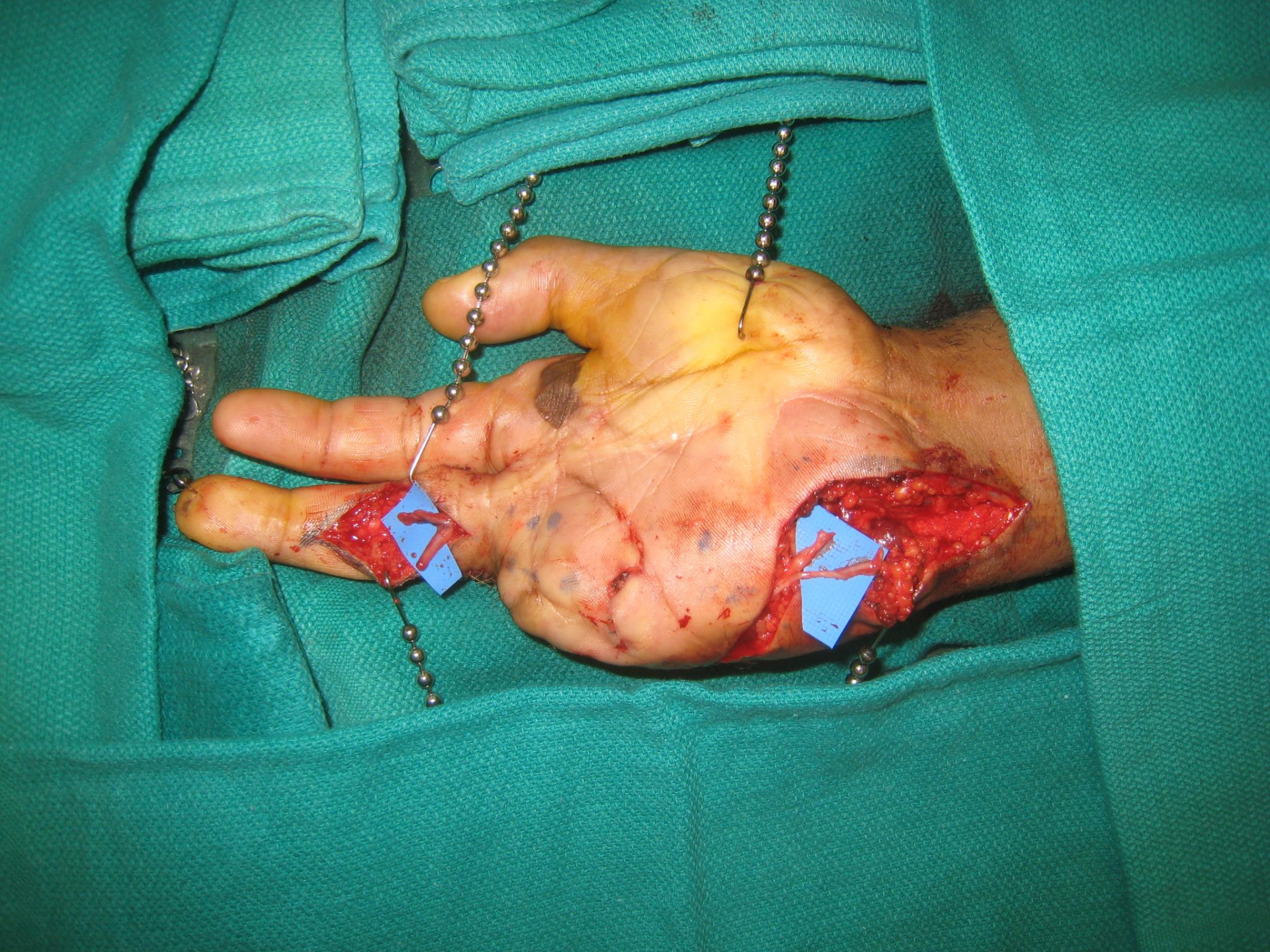



Proximal
Saphenous Vein
Distal




Cardinal Health
INCHES

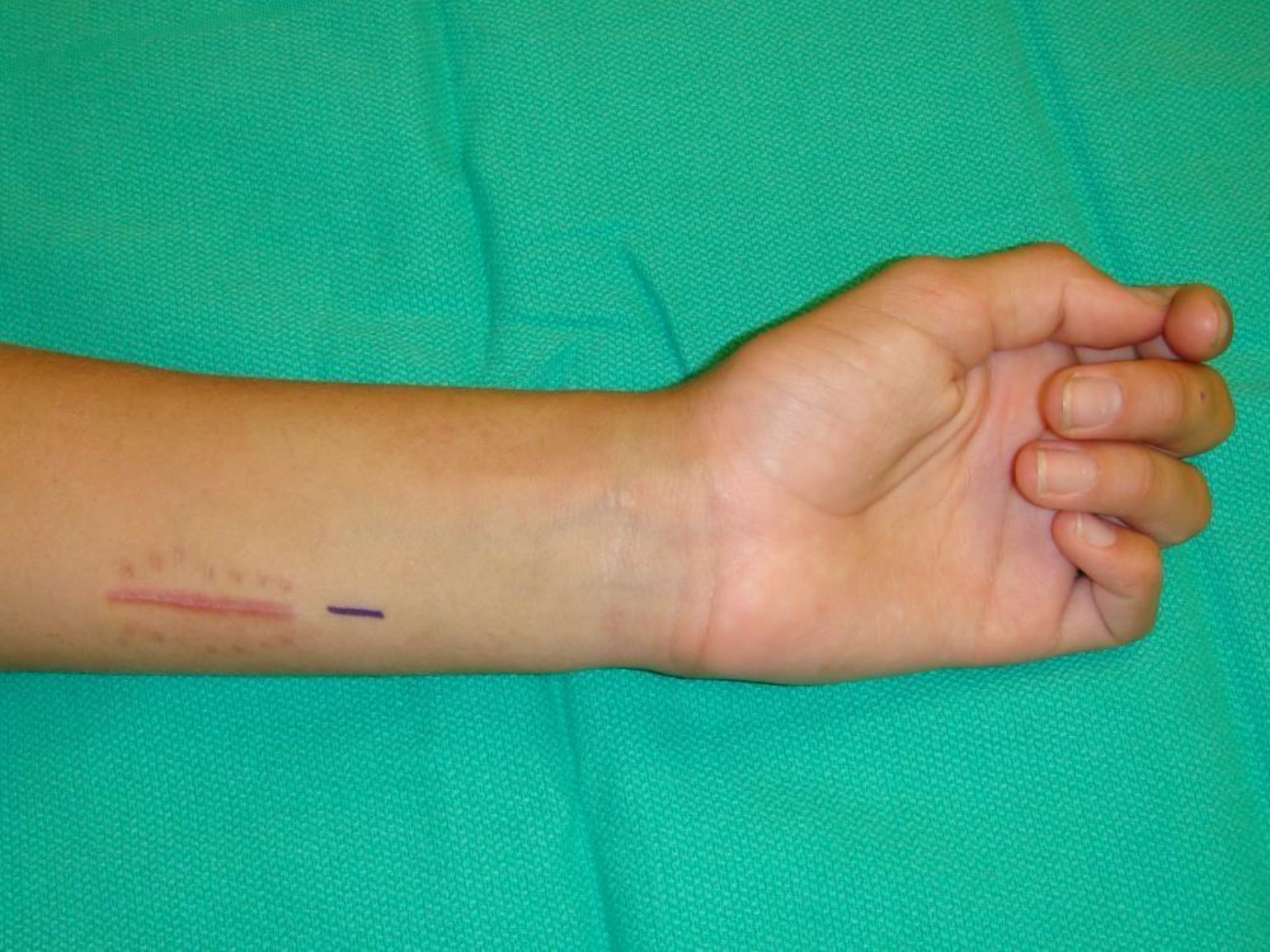


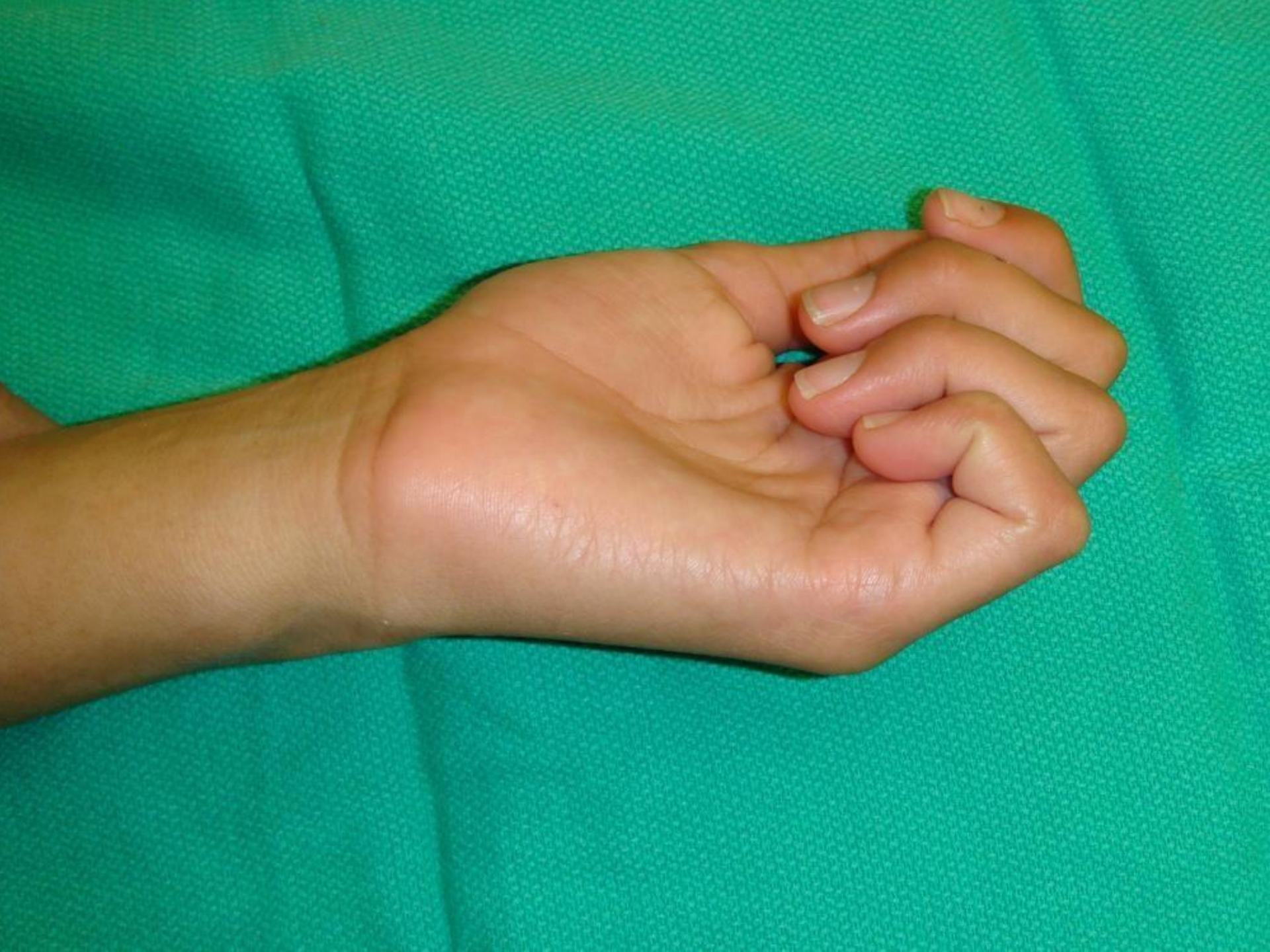

1 year

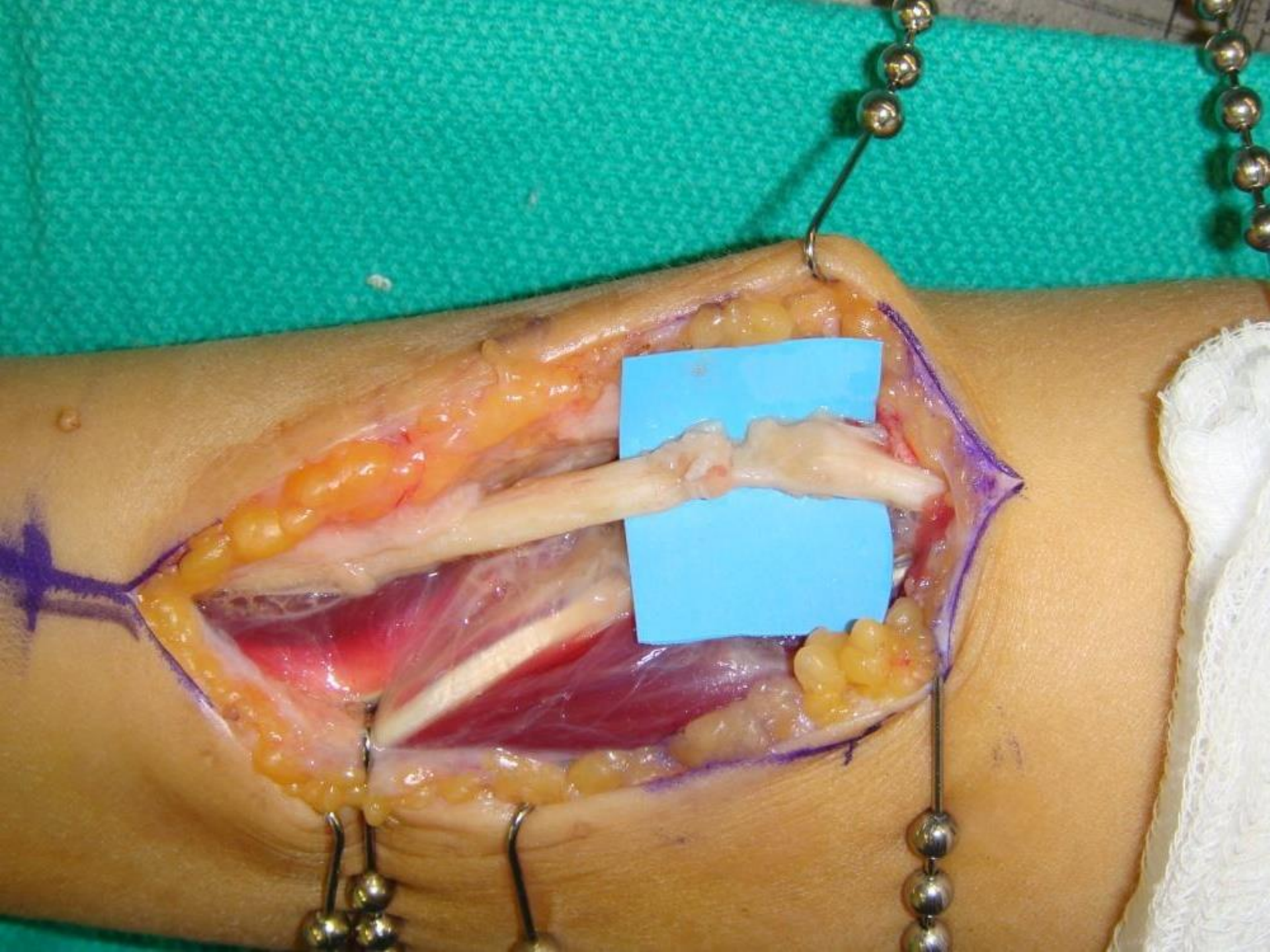

10-12mm S2PD
1 year

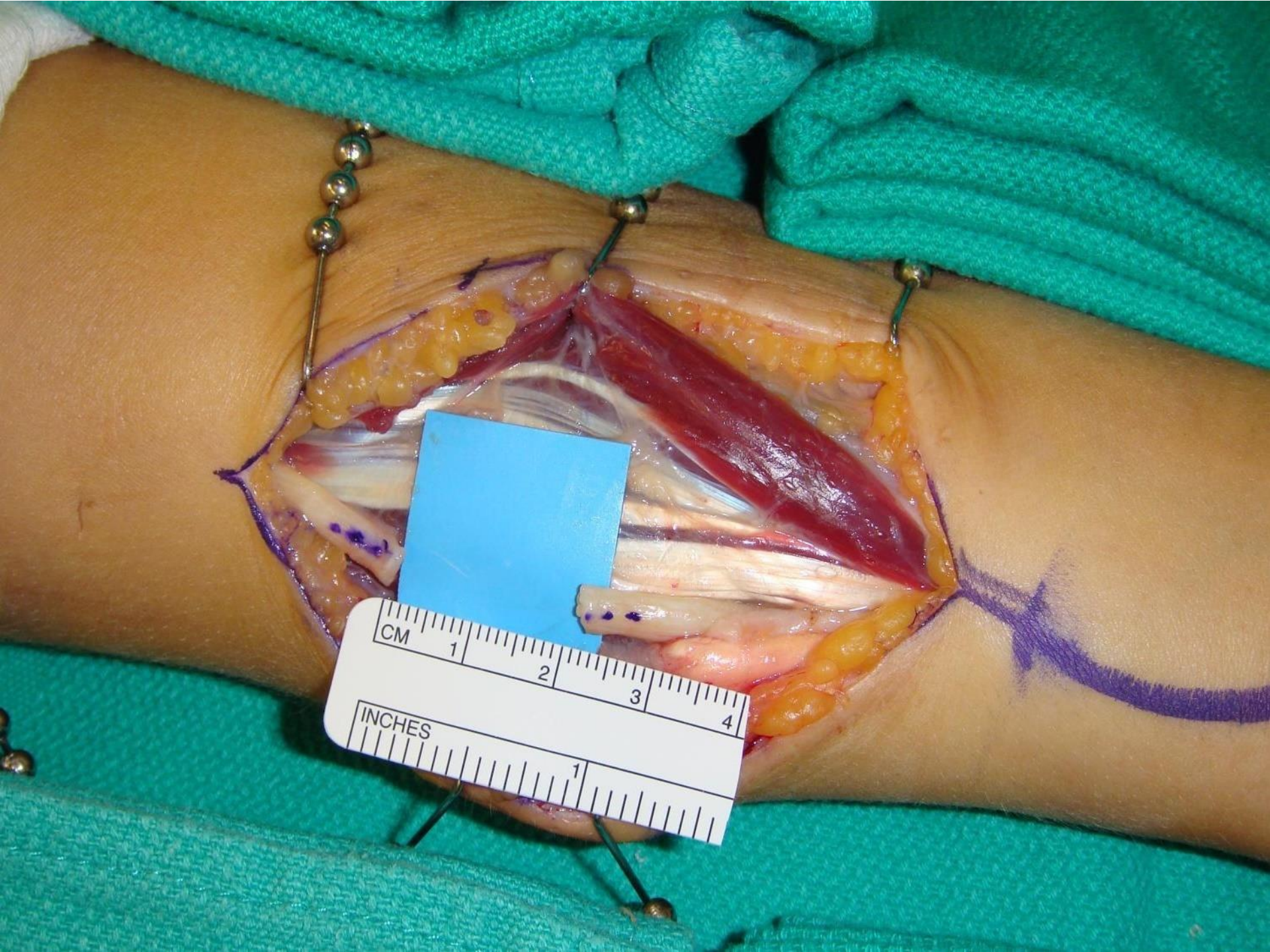


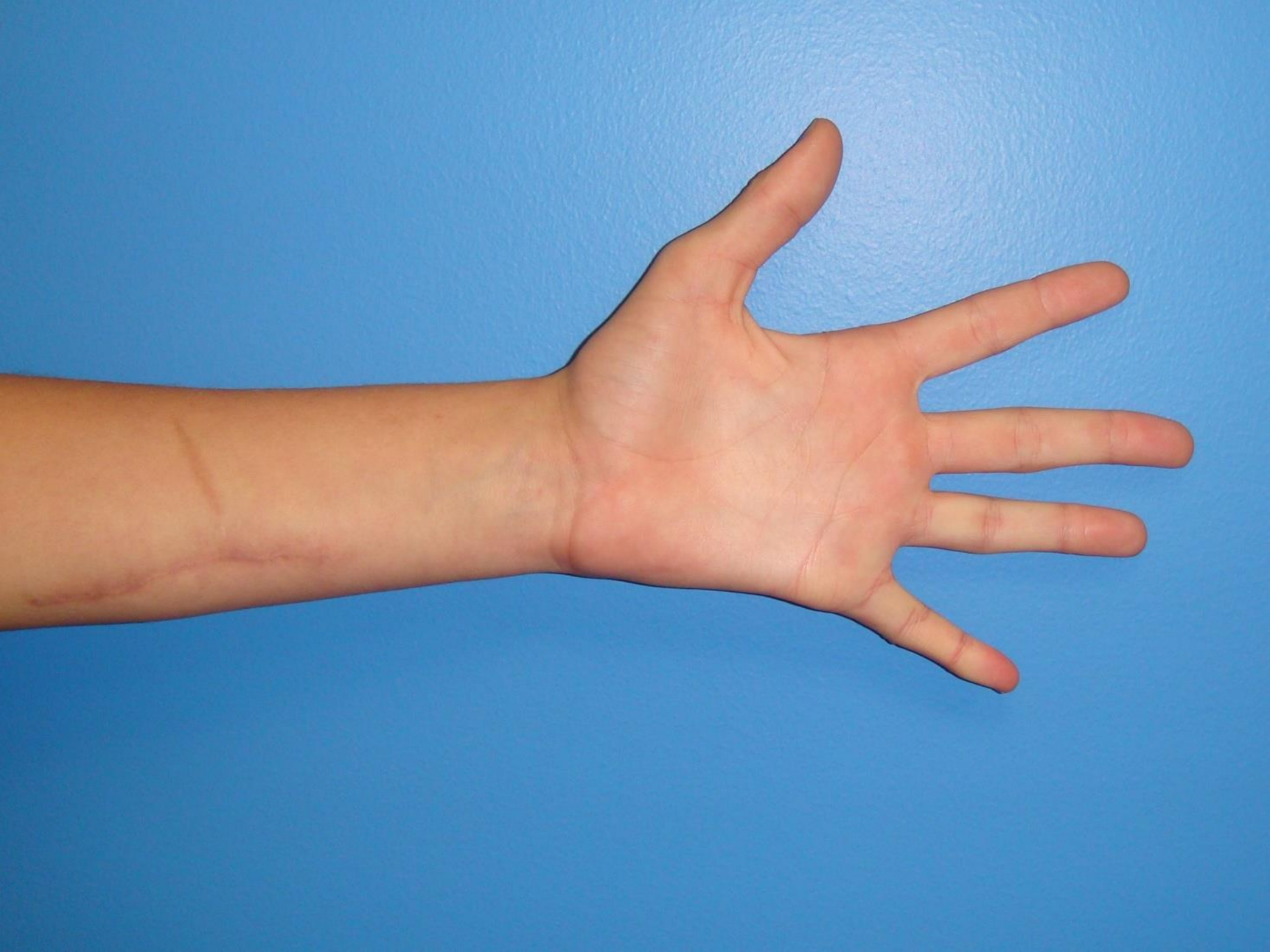
ULNAR NERVE INJURY

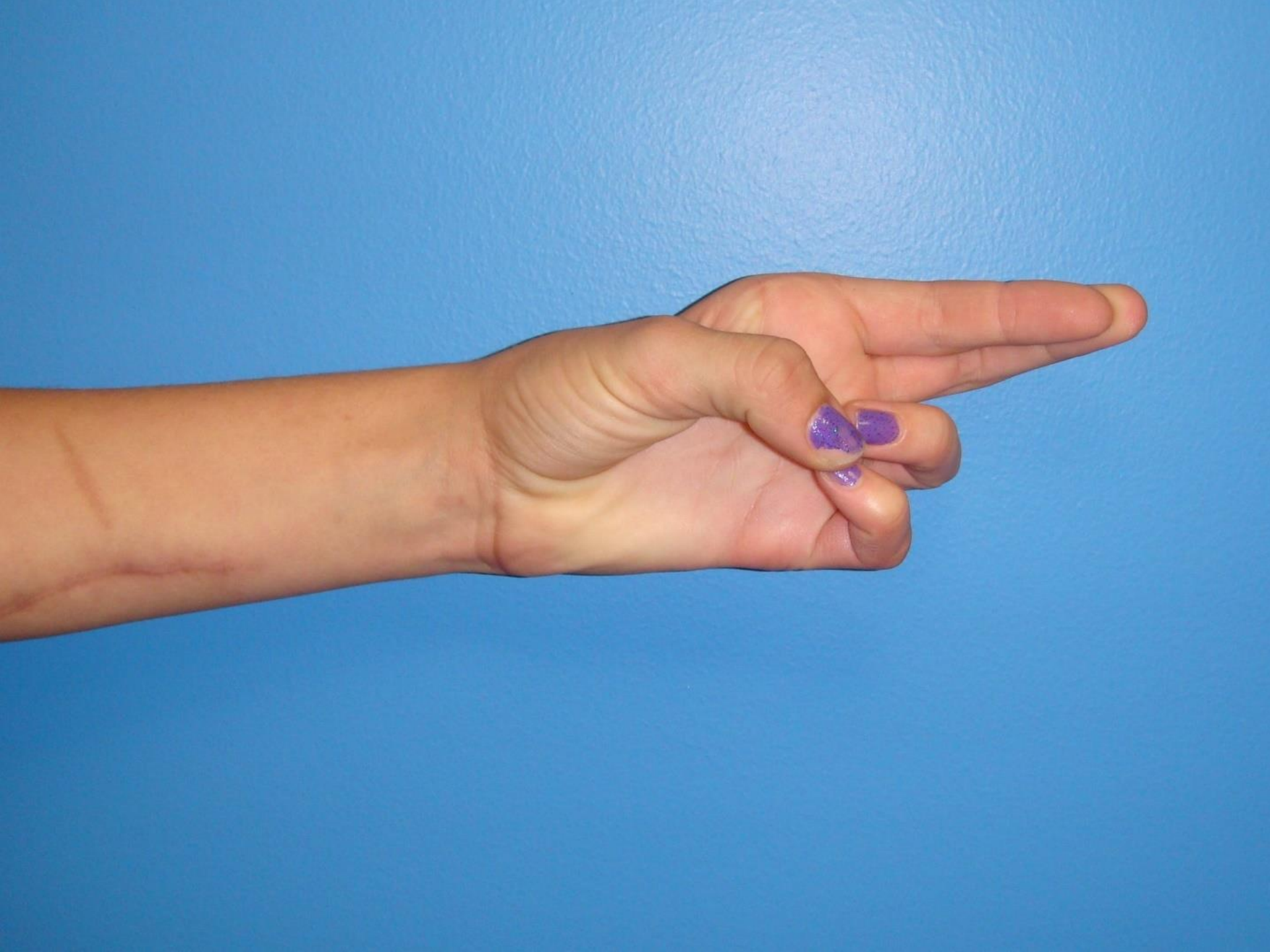


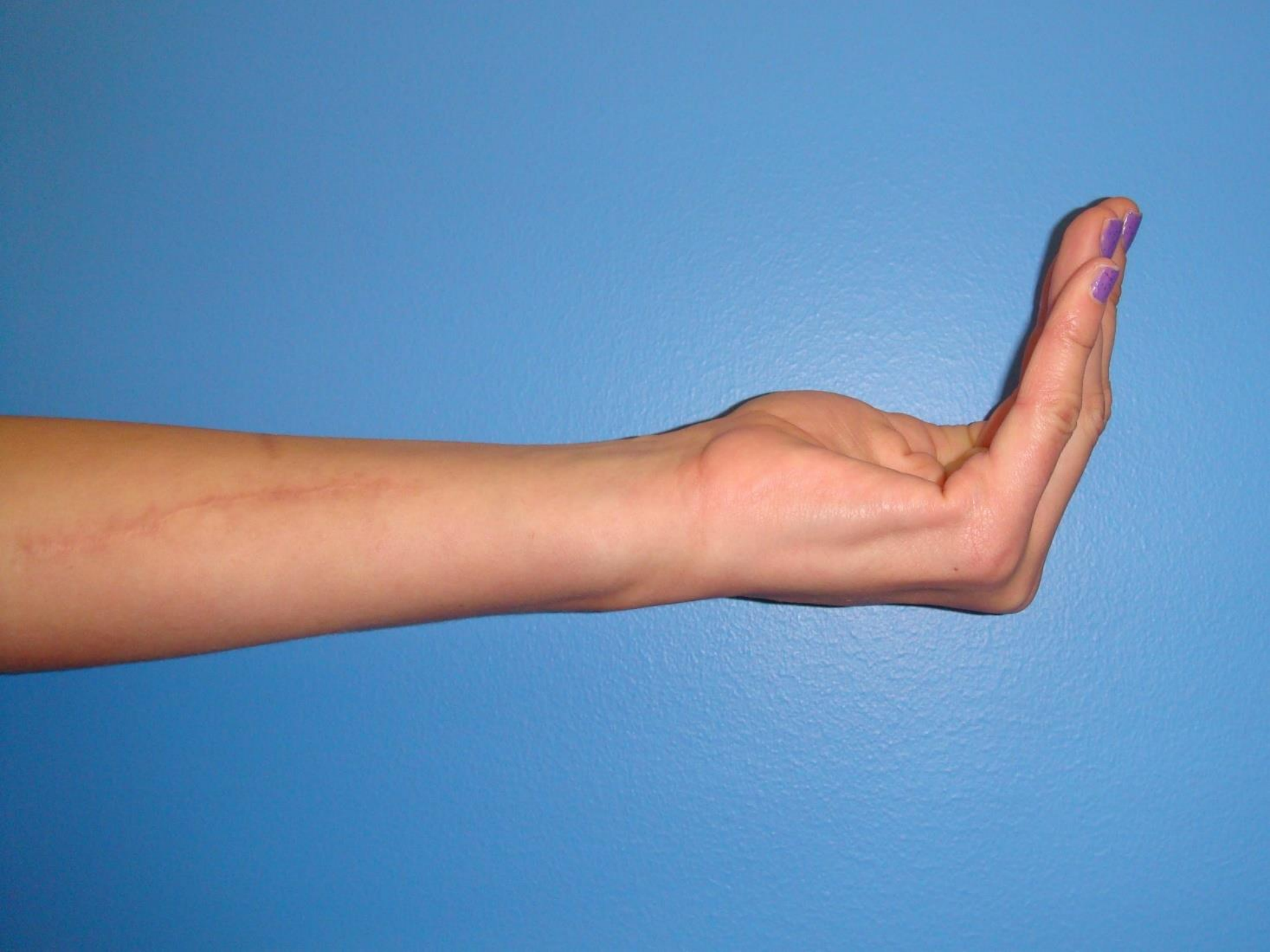





CM
1
2
3
4
INCHES
1

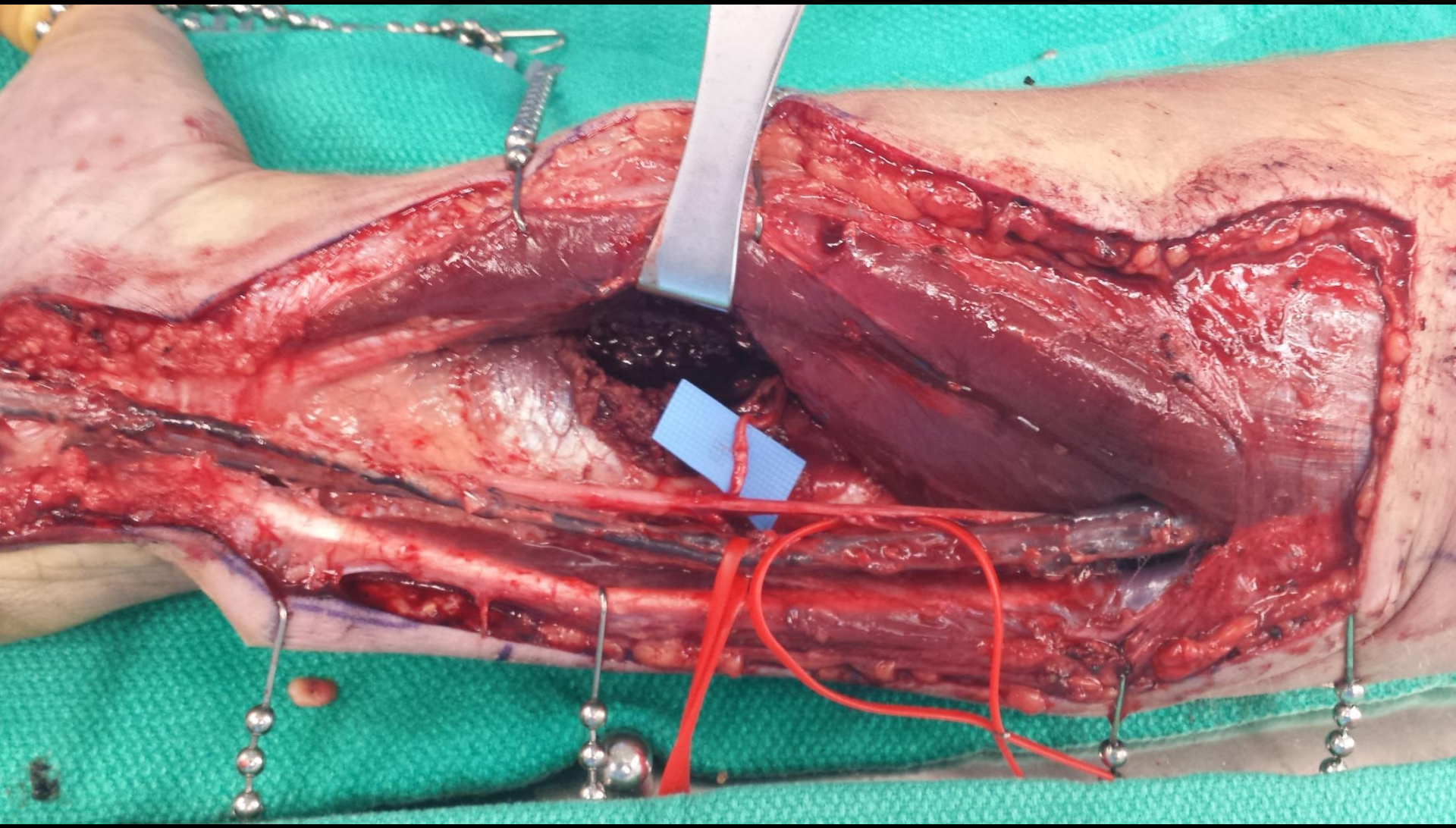




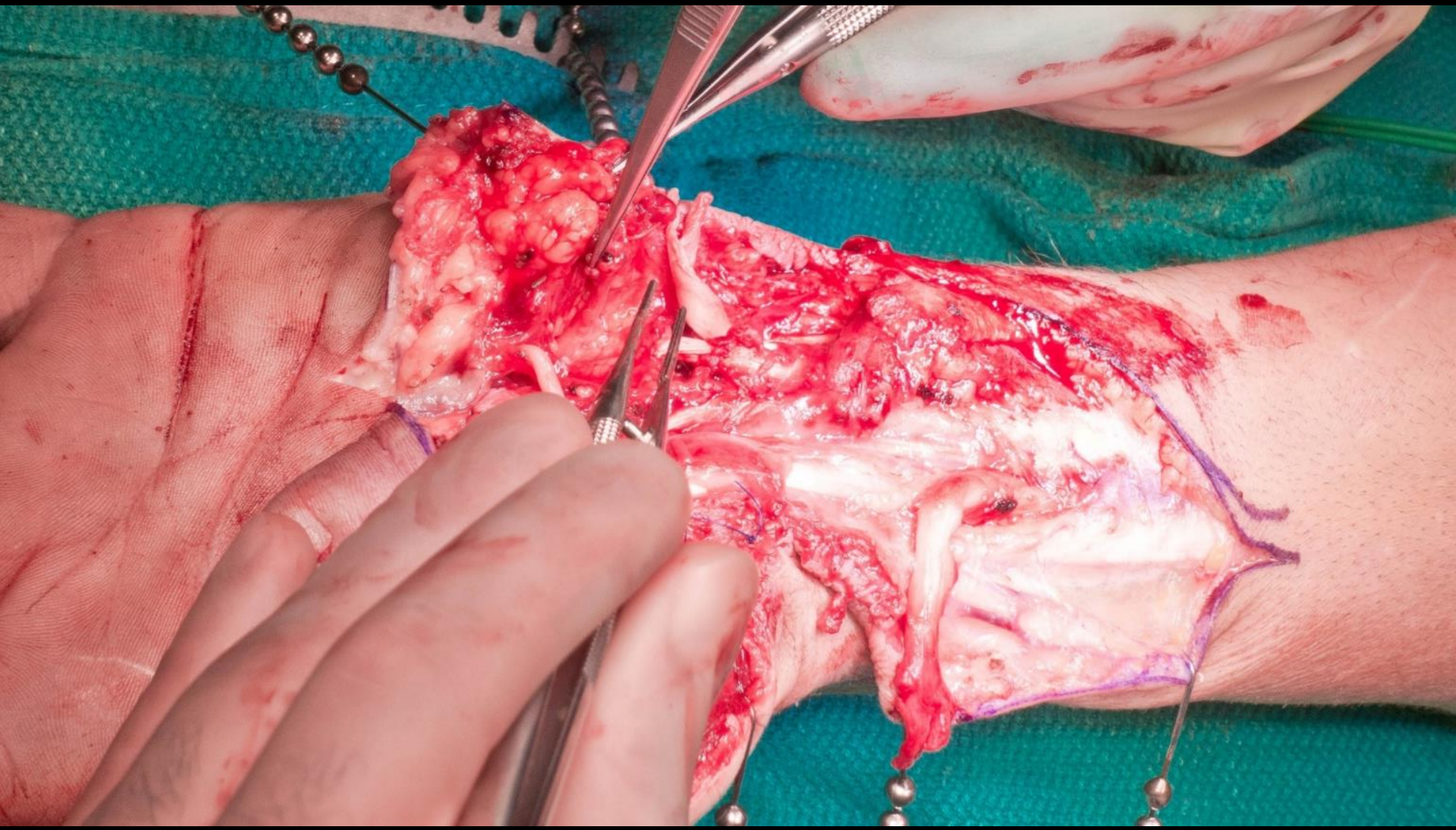


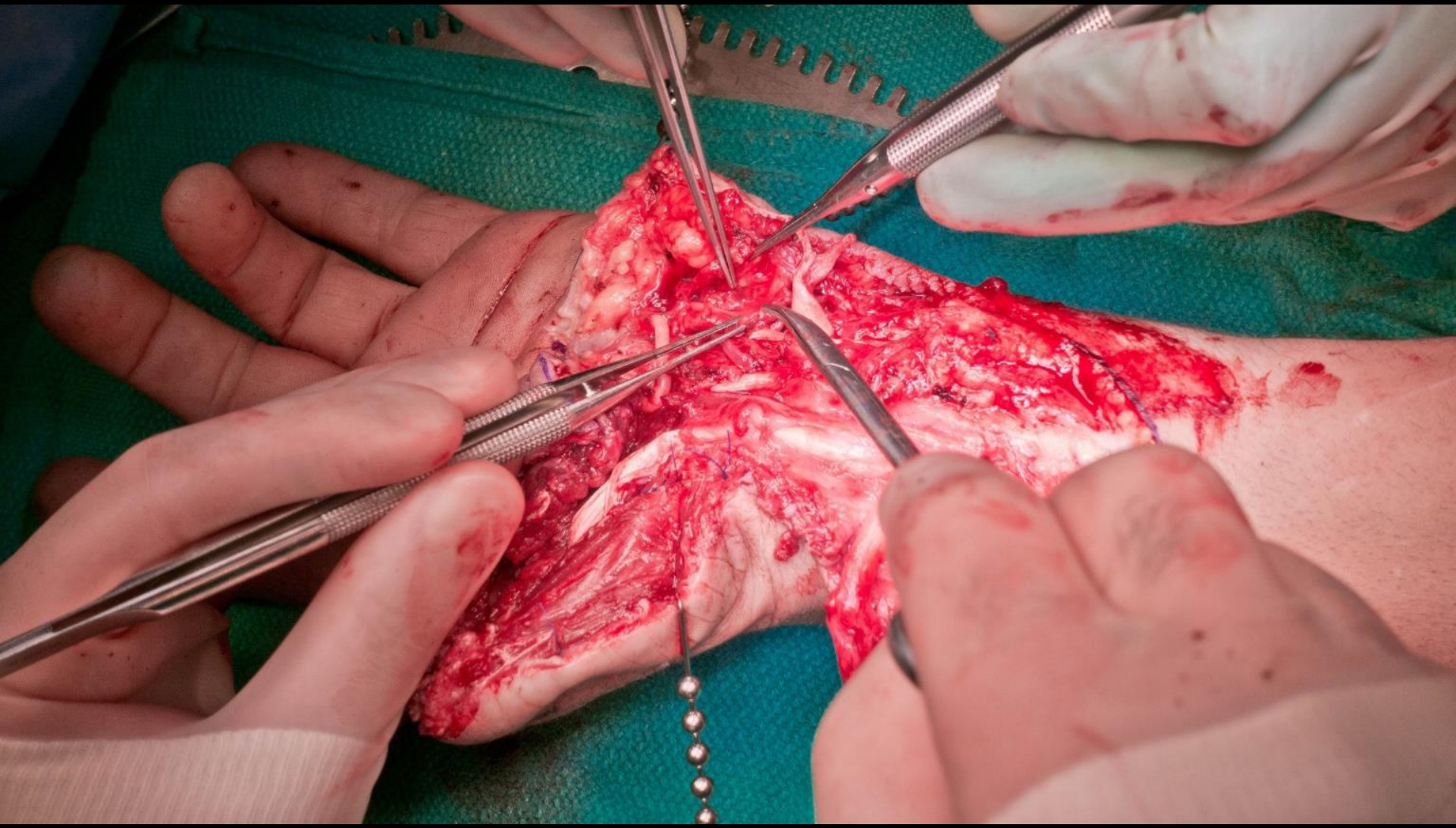
HIGH ULNAR NERVE INJURY

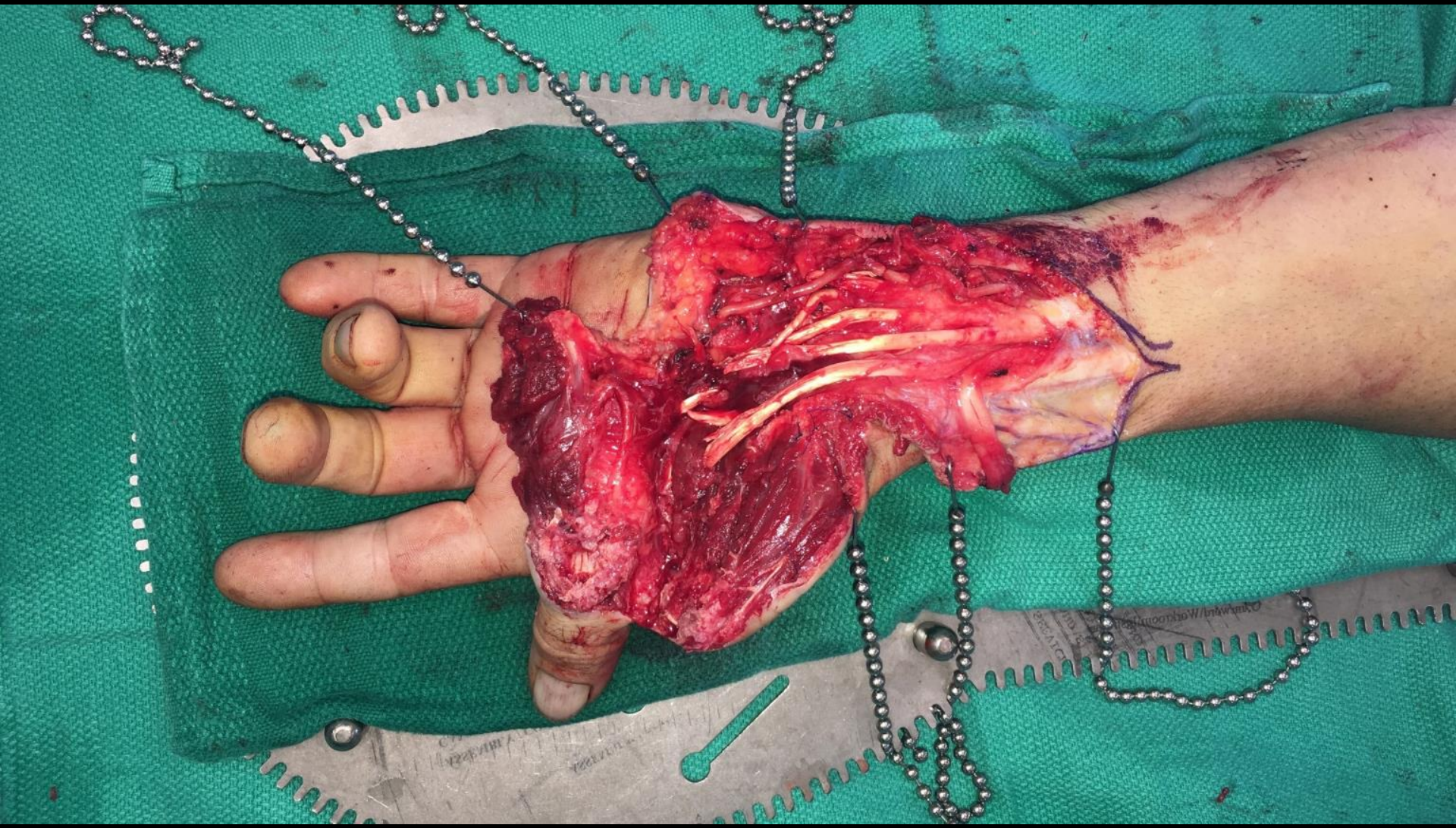

MEDLINE
INCHES
CM

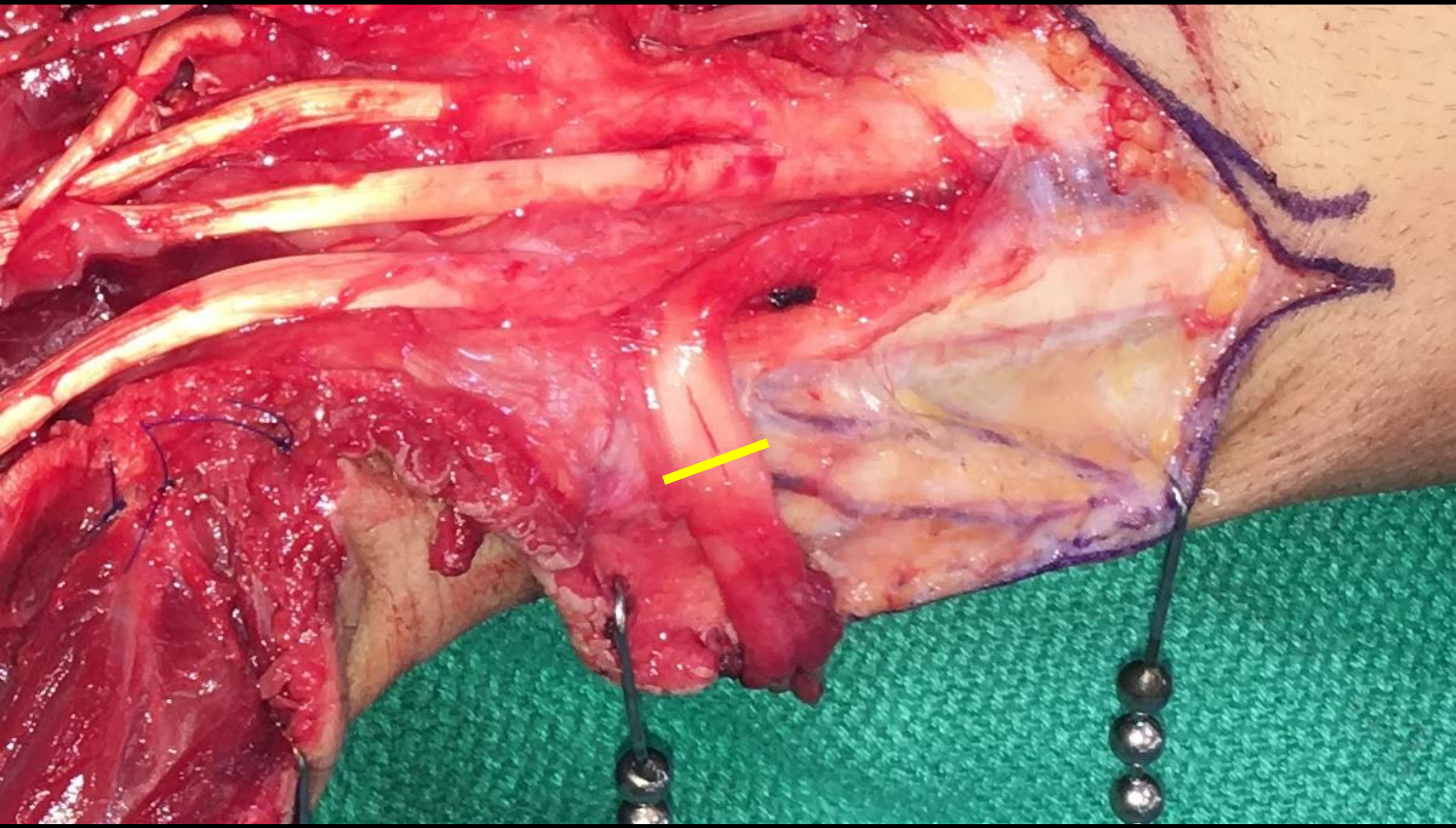


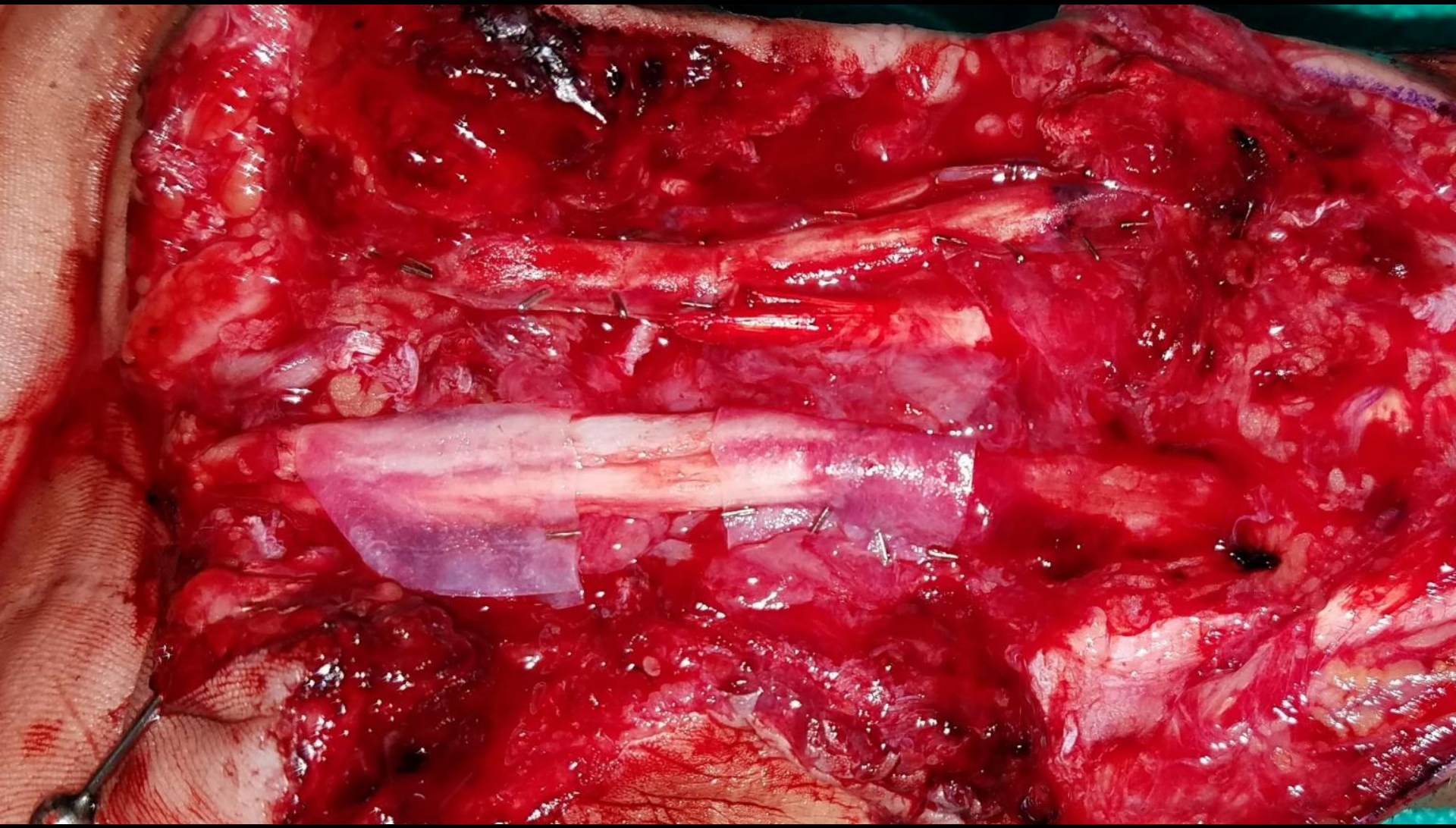

FCU function
against
strong resistance

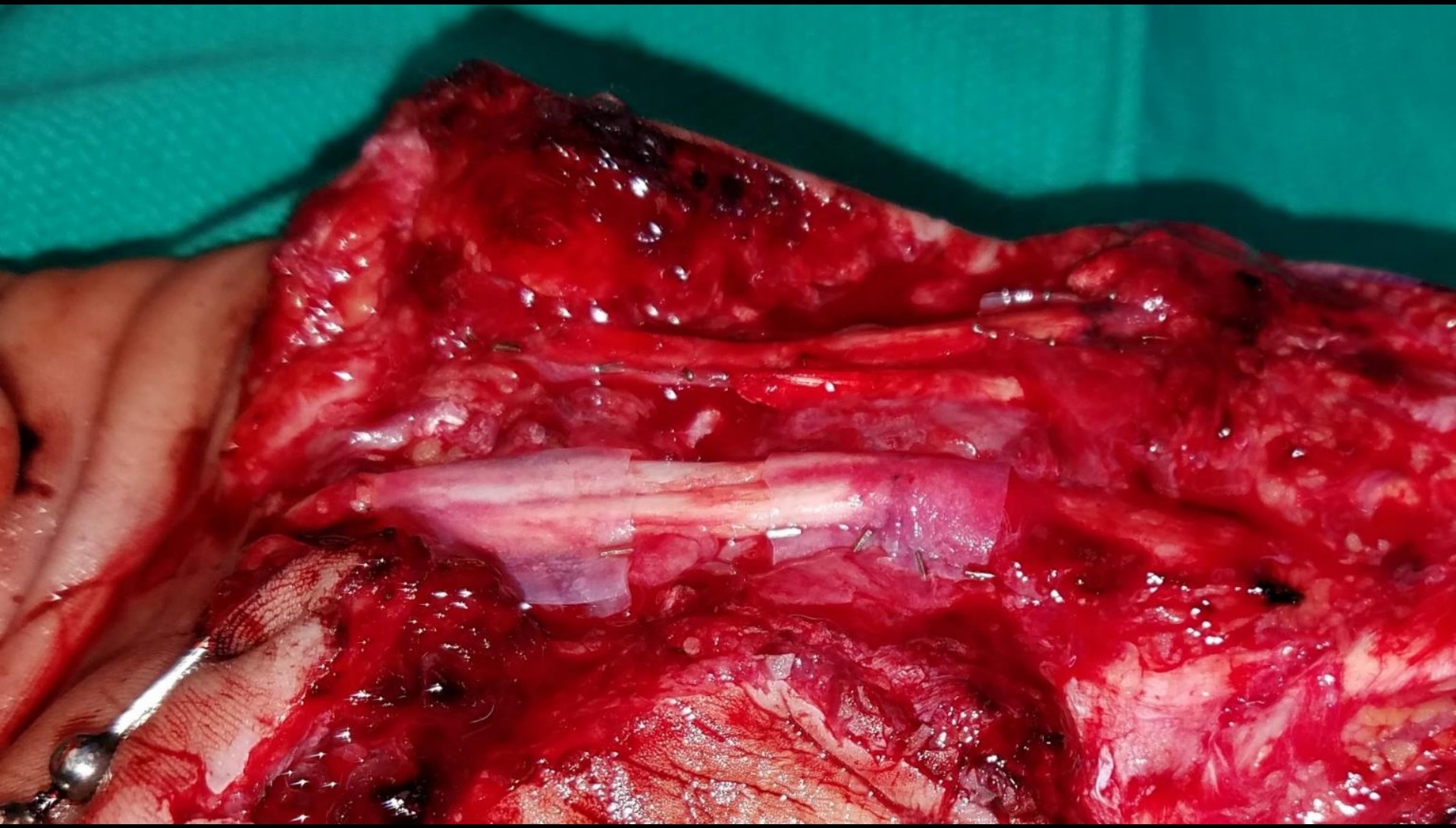






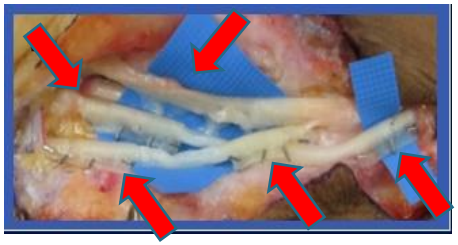






Outcomes with Processed Nerve Allograft + Nerve Protectors

- Zoldos et al. 2017 AAHS ePoster 169.
- Subgroup analysis of upper extremity nerve repairs from the RANGER Registry
- All repairs performed with peripheral nerve allograft
- Trend toward higher meaningful recovery with Protectors (89%) vs Control (79%)



Factor	PNA w/Protector	PNA only
Age (years)	43±15	43±20
No. Repairs	19	27
Follow-up (days)	361±188	409±201
Gap Length (mm)	33±14	29±11
Time to Repair		
Acute (< 3 weeks)	9	18
Delayed (3 weeks-3 mths)	5	1
Chronic (> 3 months)	5	8
Type of Nerve		
Sensory	3	5
Mixed	12	17
Motor	4	5
Mechanism of Injury		
Laceration	7	16
Complex	12	11
Meaningful Recovery	**89%***	**79%***

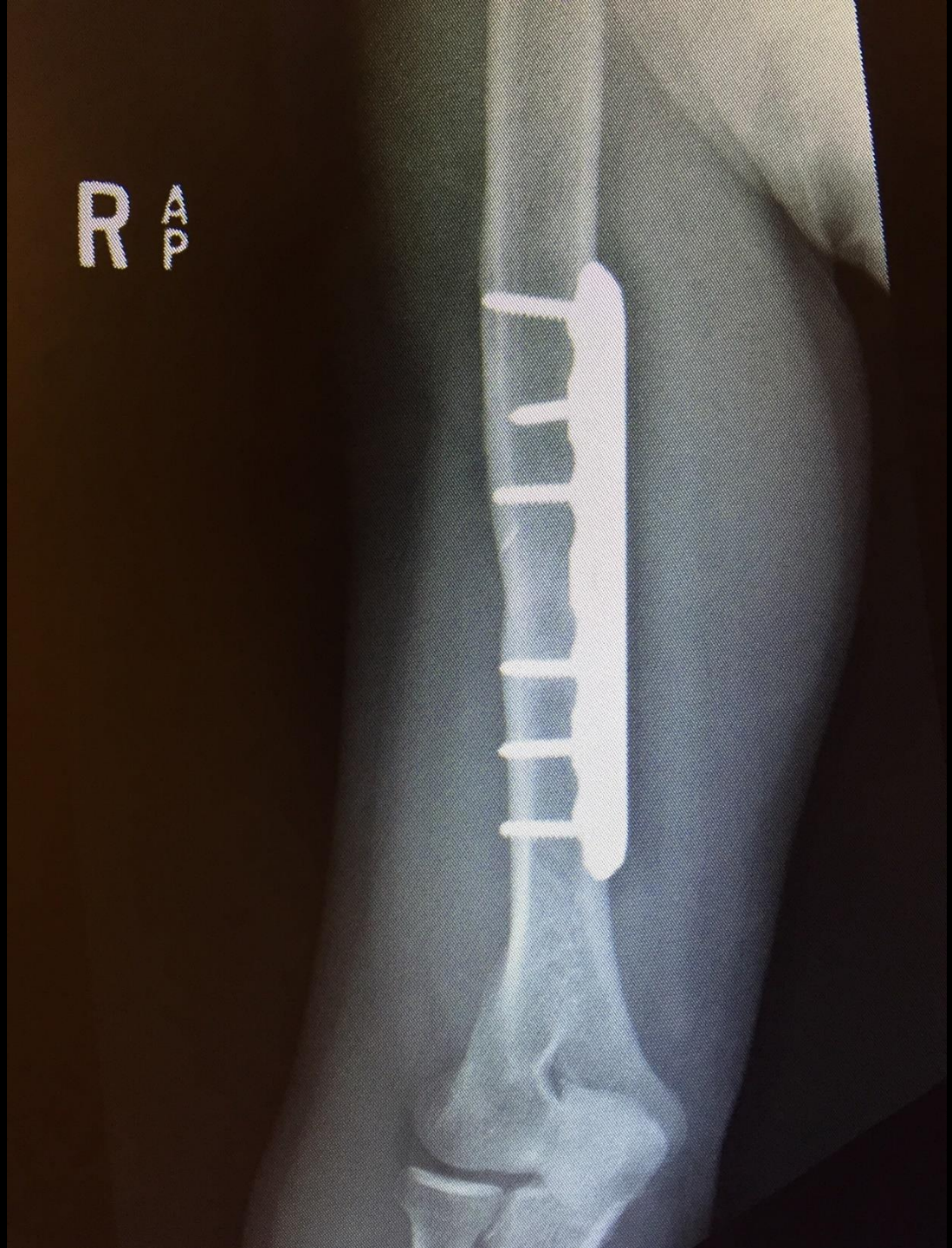
*p=0.26, Fisher's exact test
Age, follow-up days and gap length are presented as Mean±SD

6 Months Post-Op

RADIAL NERVE INJURY

CASE 3

- Radial nerve defect associated with humerus fx
- 3-4cm gap bridged with 5cm allograft


R
AP

- 15 months
- WE = 4/5
- finger ext = 3+ to 4- /5
- 2-3cm gap bridged with 5cm allograft

- 15 months
- WE = 4/5
- finger ext = 3+ to 4- /5
- 2-3cm gap bridged with 5cm allograft

- 15 months
- WE = 4/5
- finger ext = 3+ to 4- /5
- 2-3cm gap bridged with 5cm allograft

- 20 months
- WE = 4+/5
- finger ext = 4/5 → EIP returned
- Sensation “80%” normal SBRN

- 20 months
- WE = 4+/5
- finger ext = 4/5 → EIP returned
- Sensation “80%” normal SBRN

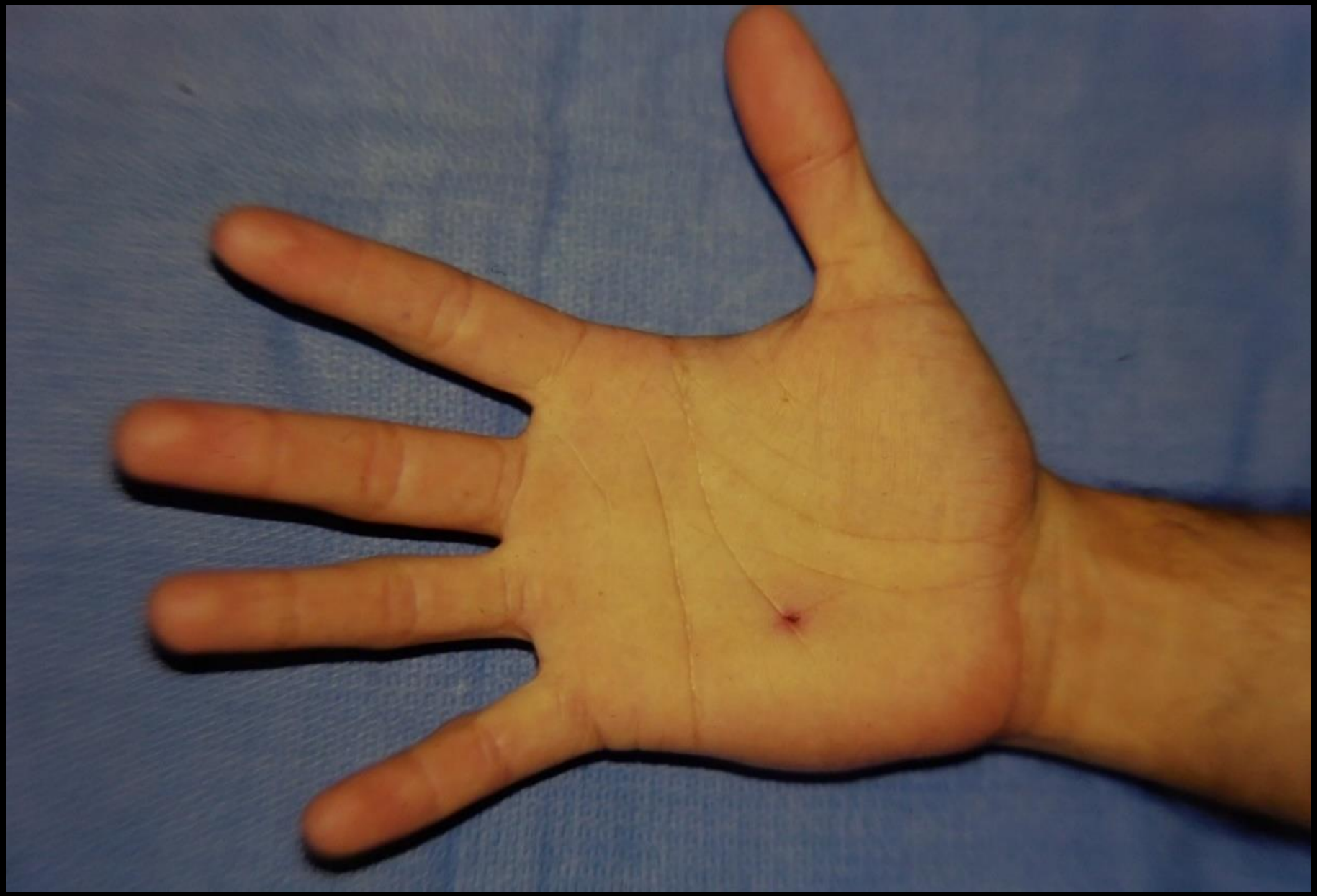
DEEP ULNAR MOTOR NERVE INJURY

CASE 4

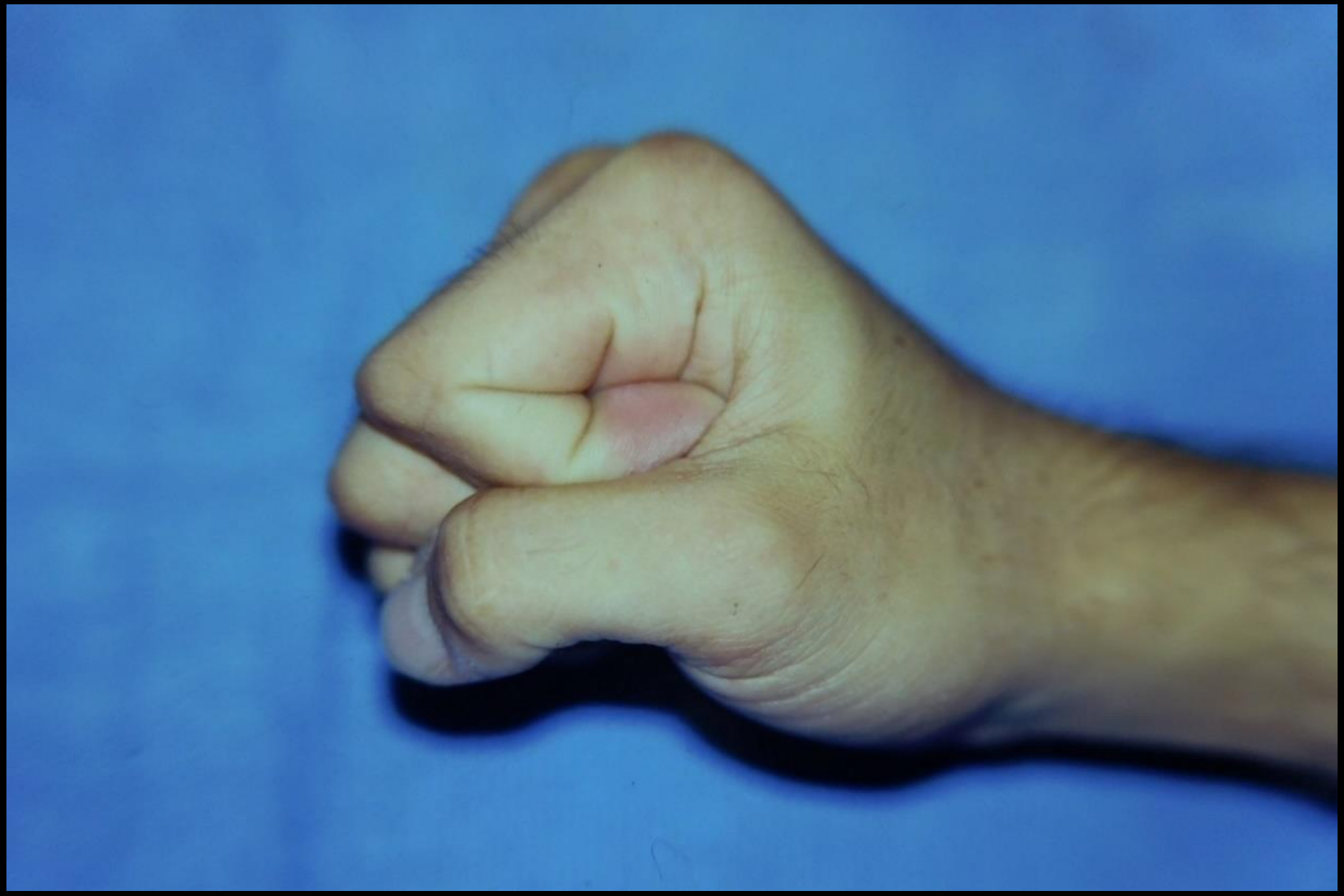
Ice Pick Injury

- 45 year old male
- Ice pick injury to right hand
- Specific, isolated ulnar motor deficit
- No sensory loss

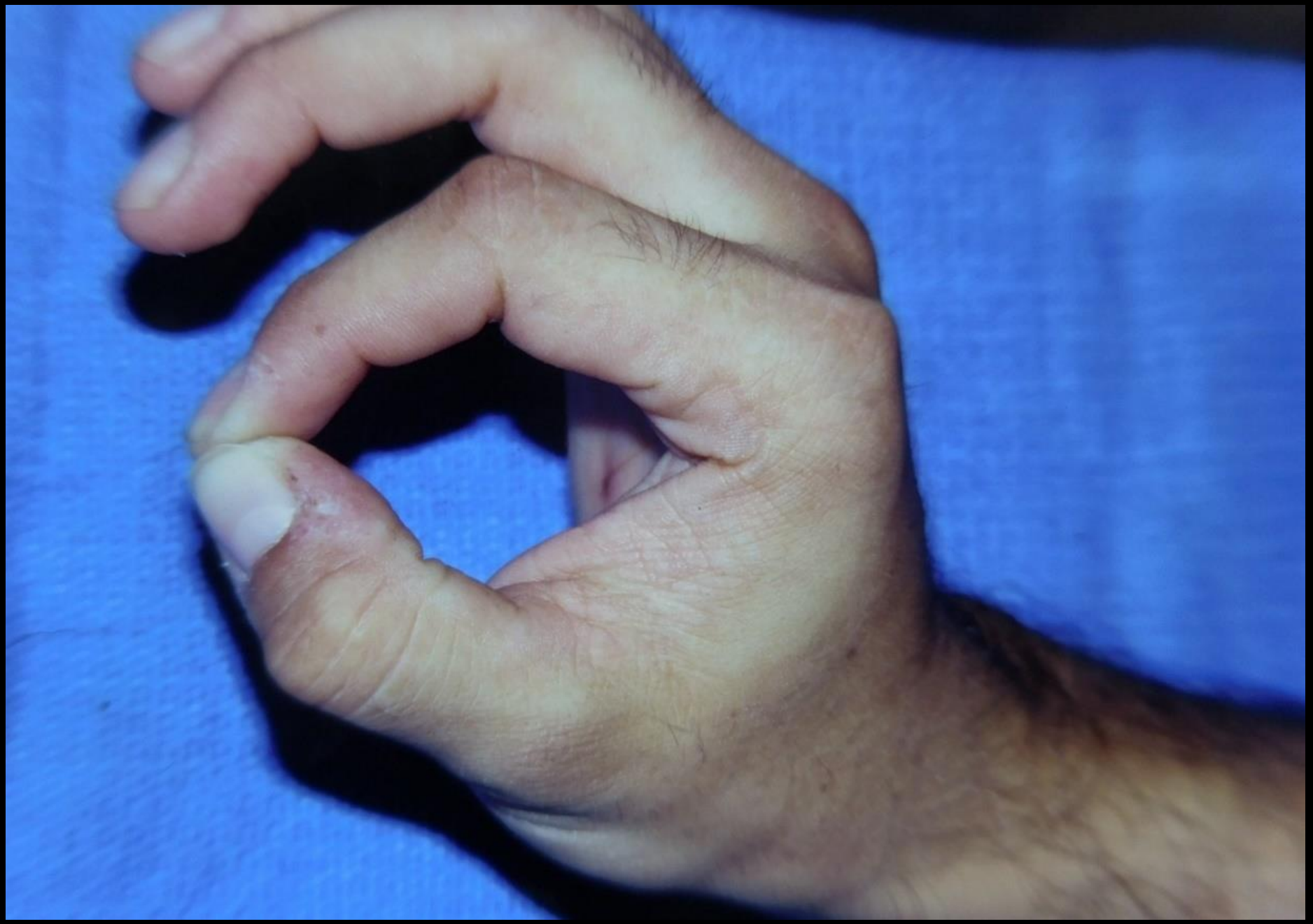
Courtesy: Prosper Benhaim, MD



Courtesy: Prosper Benhaim, MD



Courtesy: Prosper Benhaim, MD



Courtesy: Prosper Benhaim, MD

Courtesy: Prosper Benhaim, MD

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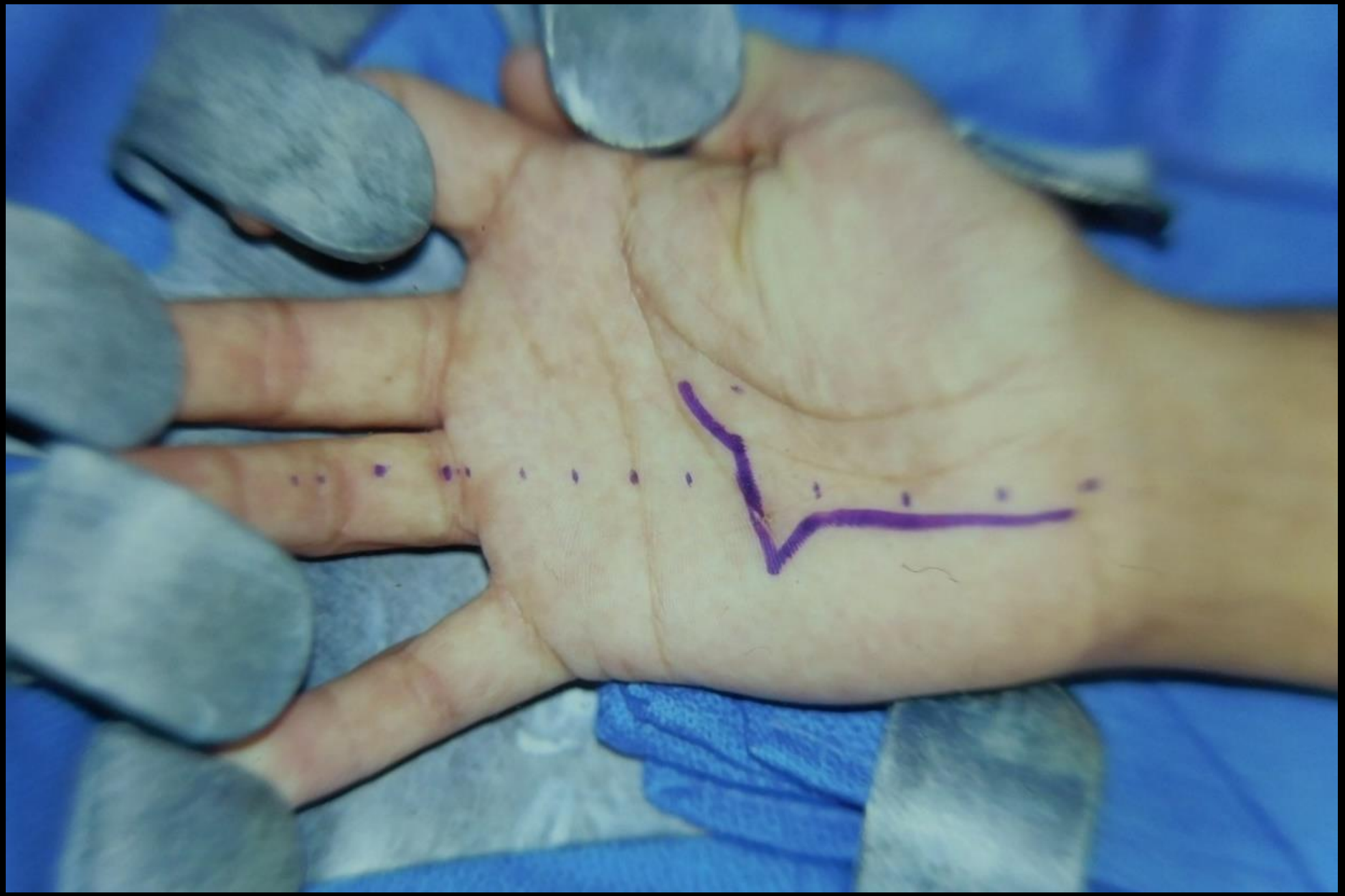


Courtesy: Prosper Benhaim, MD

Courtesy: Prosper Benhaim, MD

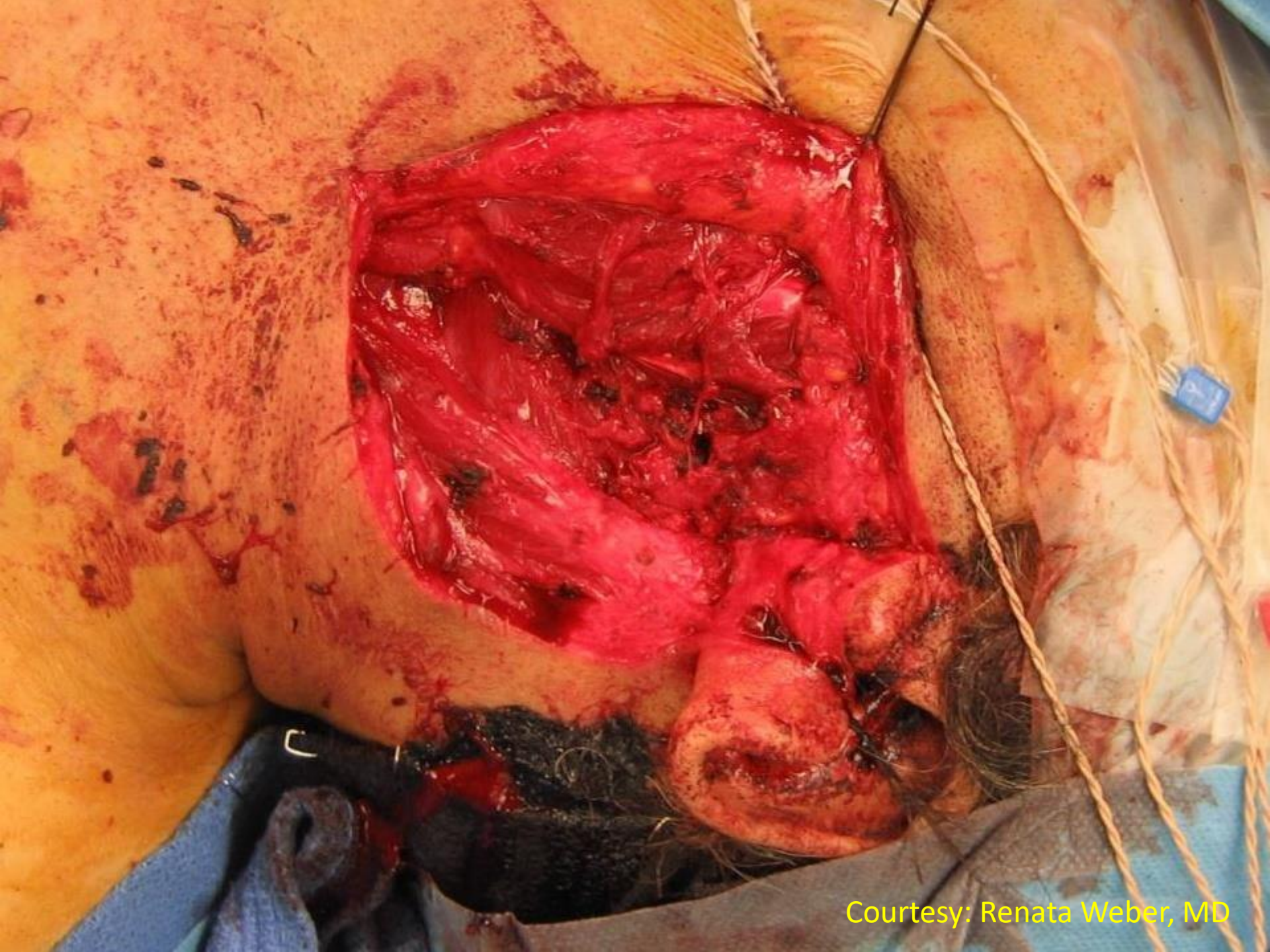
Courtesy: Prosper Benhaim, MD

Courtesy: Prosper Benhaim, MD

Courtesy: Prosper Benhaim, MD

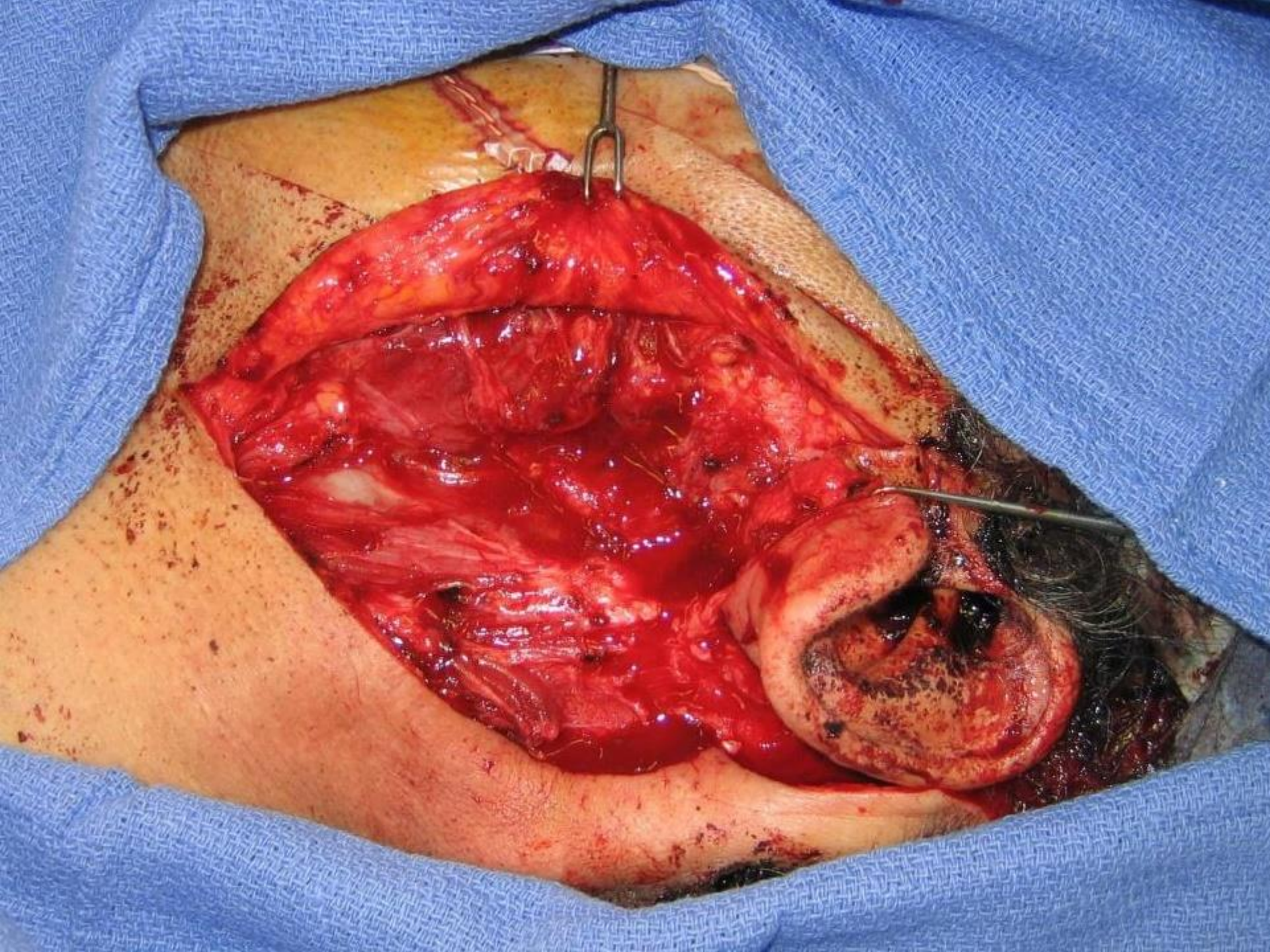
FACIAL NERVE

CASE 5


Courtesy: Renata Weber, MD

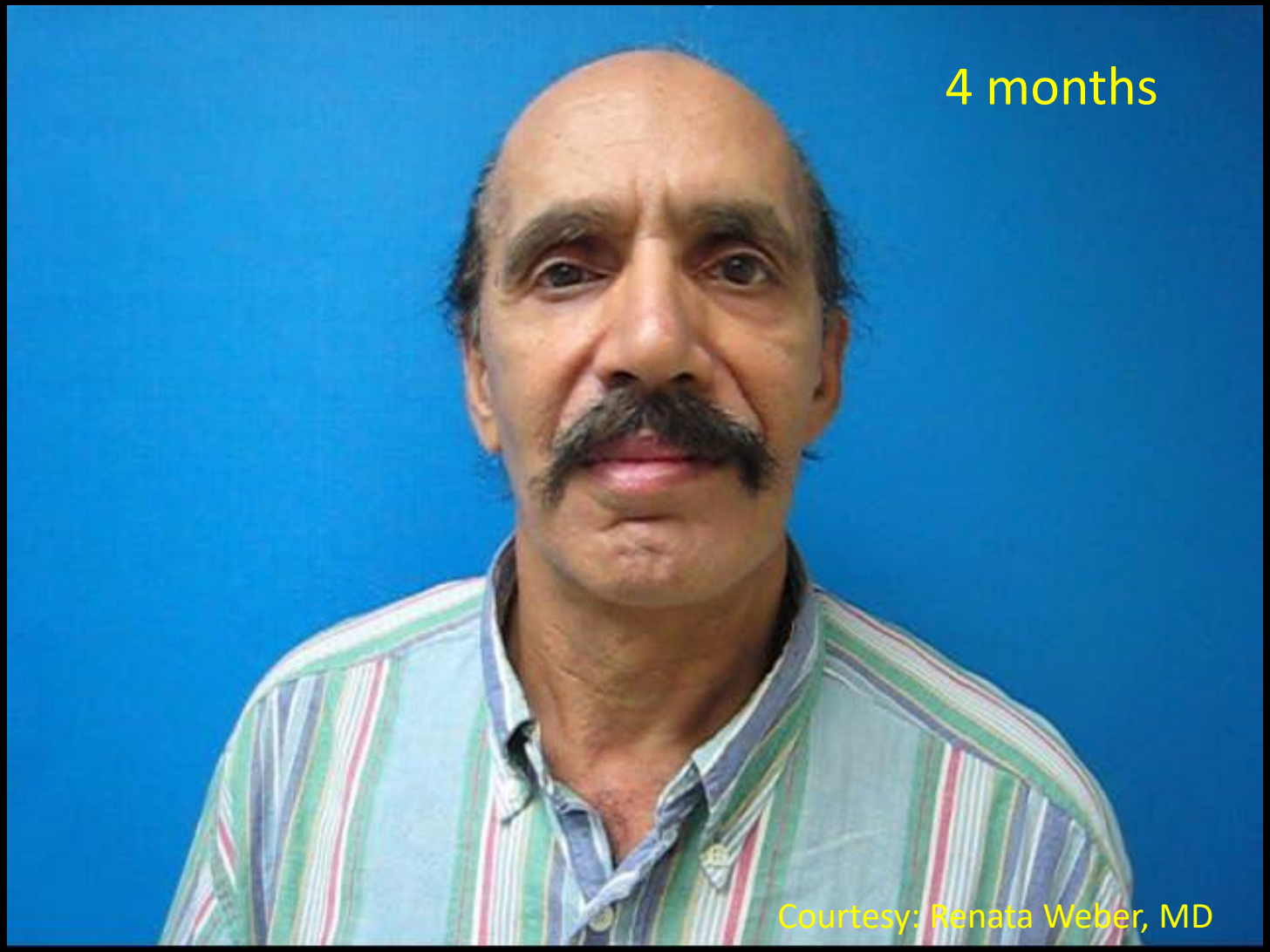
Defects

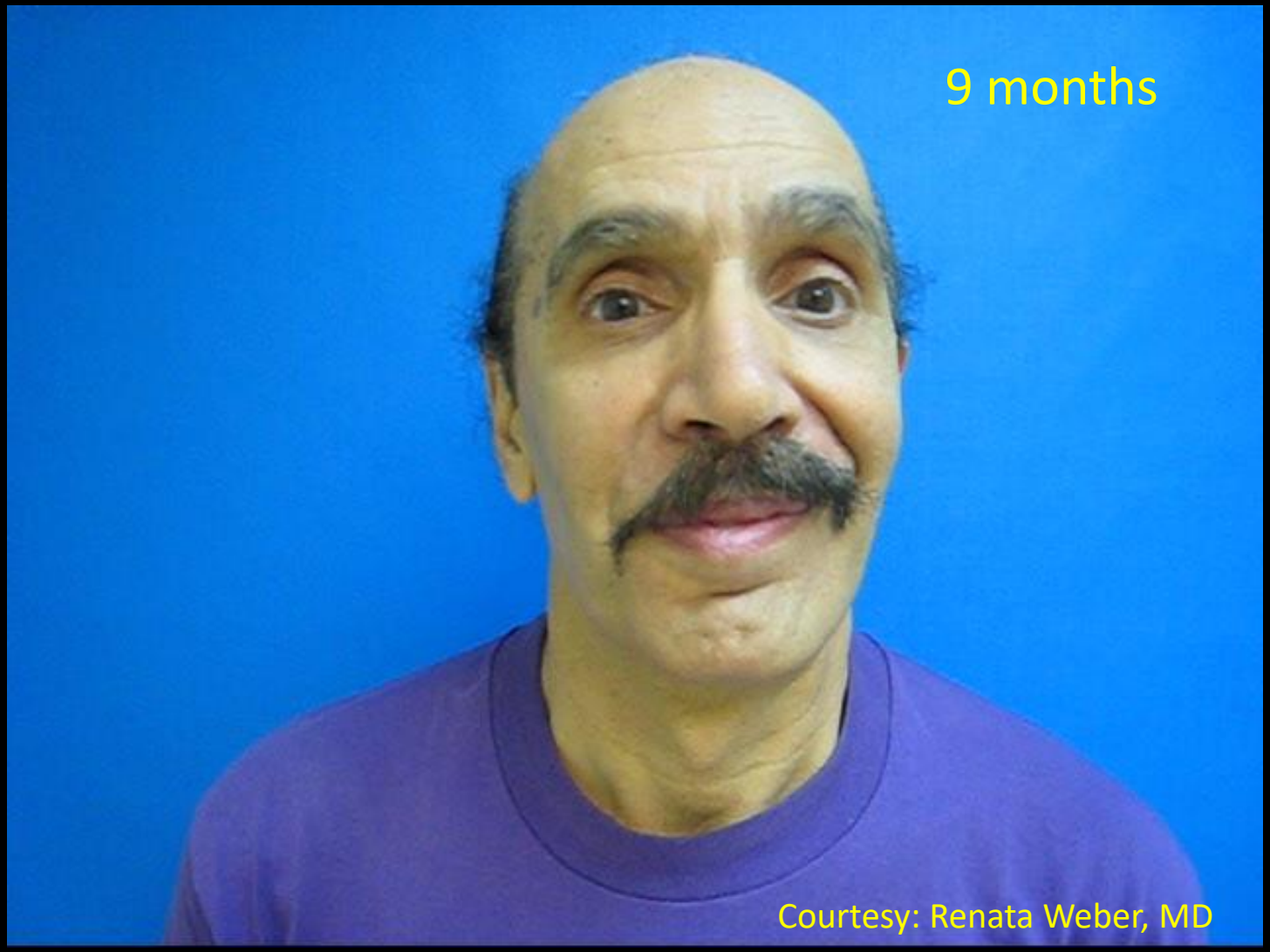
- Marginal mandibular
- Buccal
- Zygomatic
- (Frontal/temporal intact)



Motor Nerve Results

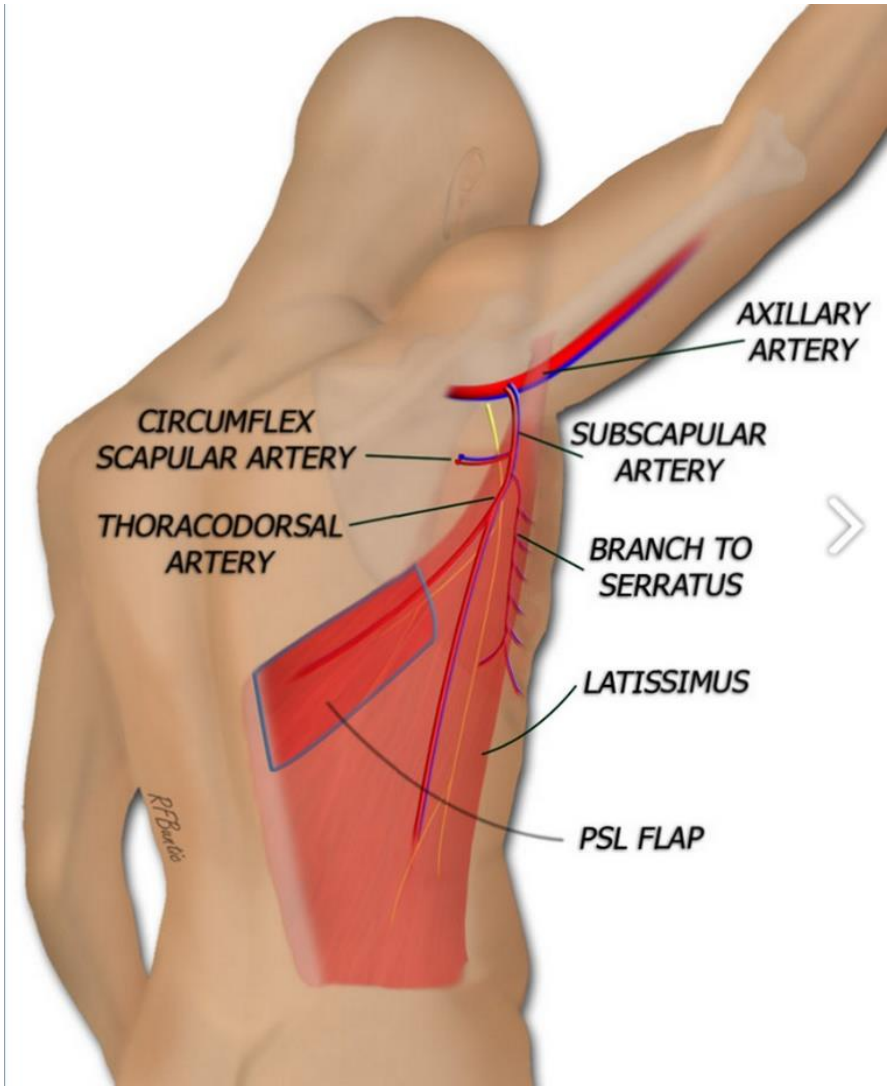
- Defects in:
  - Marginal mandibular
  - Buccal
  - Zygomatic
  - (Frontal/temporal intact)
- 30 mm x2, 40mm x1 lower Facial nerve branches
  - At 4 months, zygomatic & buccal branches recovered
  - At 9 months, marginal mandibular and ungrafted upper branches fully recovered.

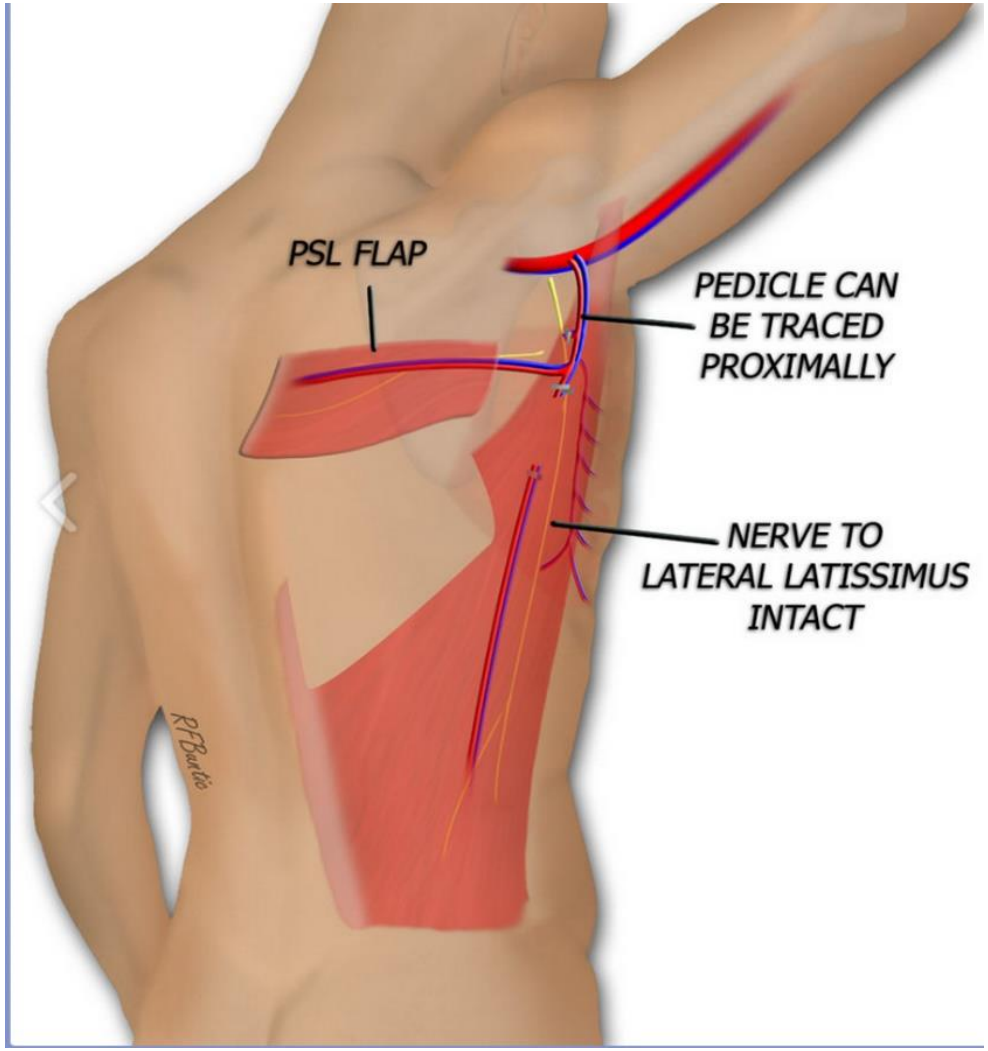

4 months
Courtesy: Renata Weber, MD

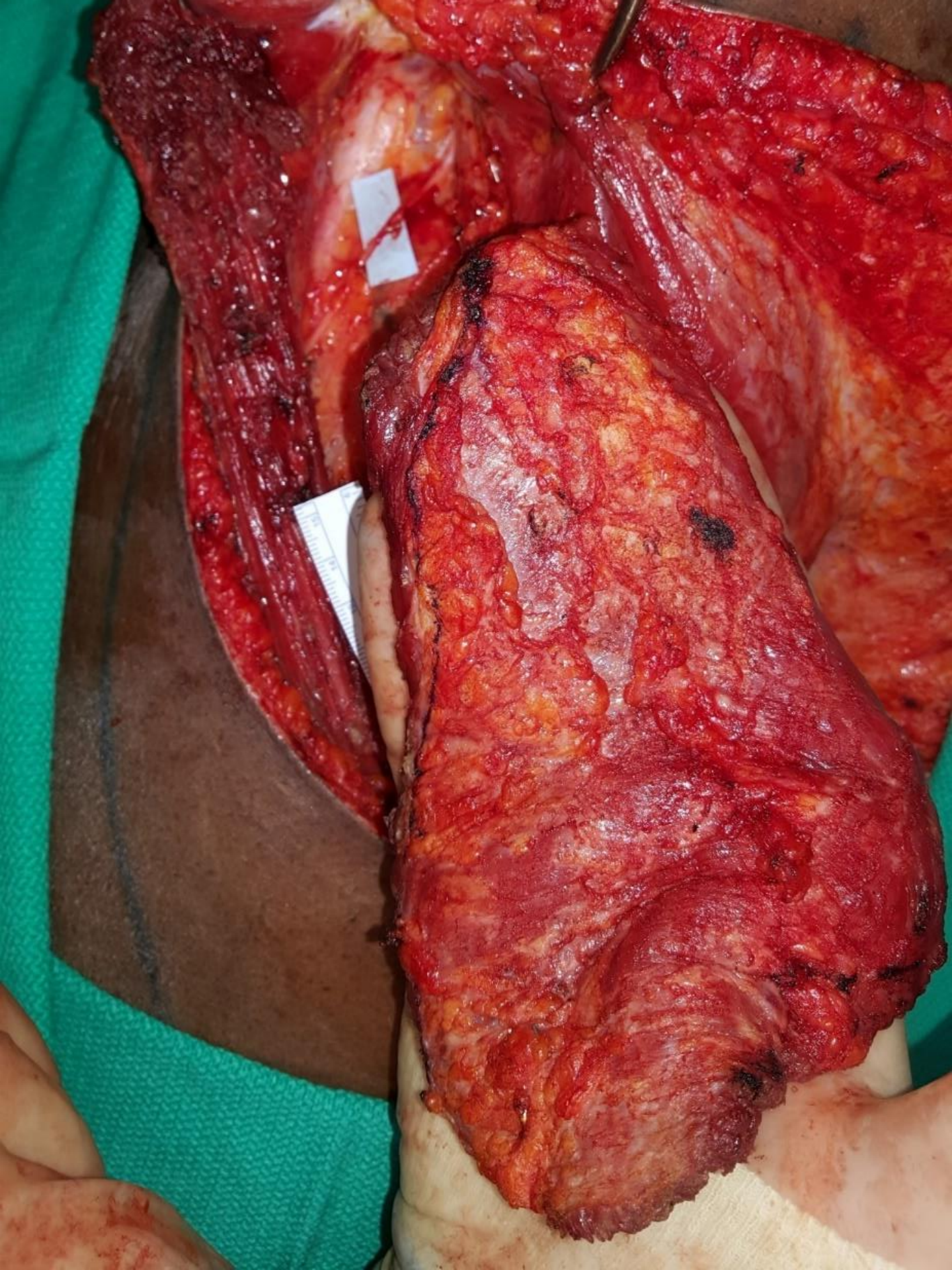

9 months
Courtesy: Renata Weber, MD

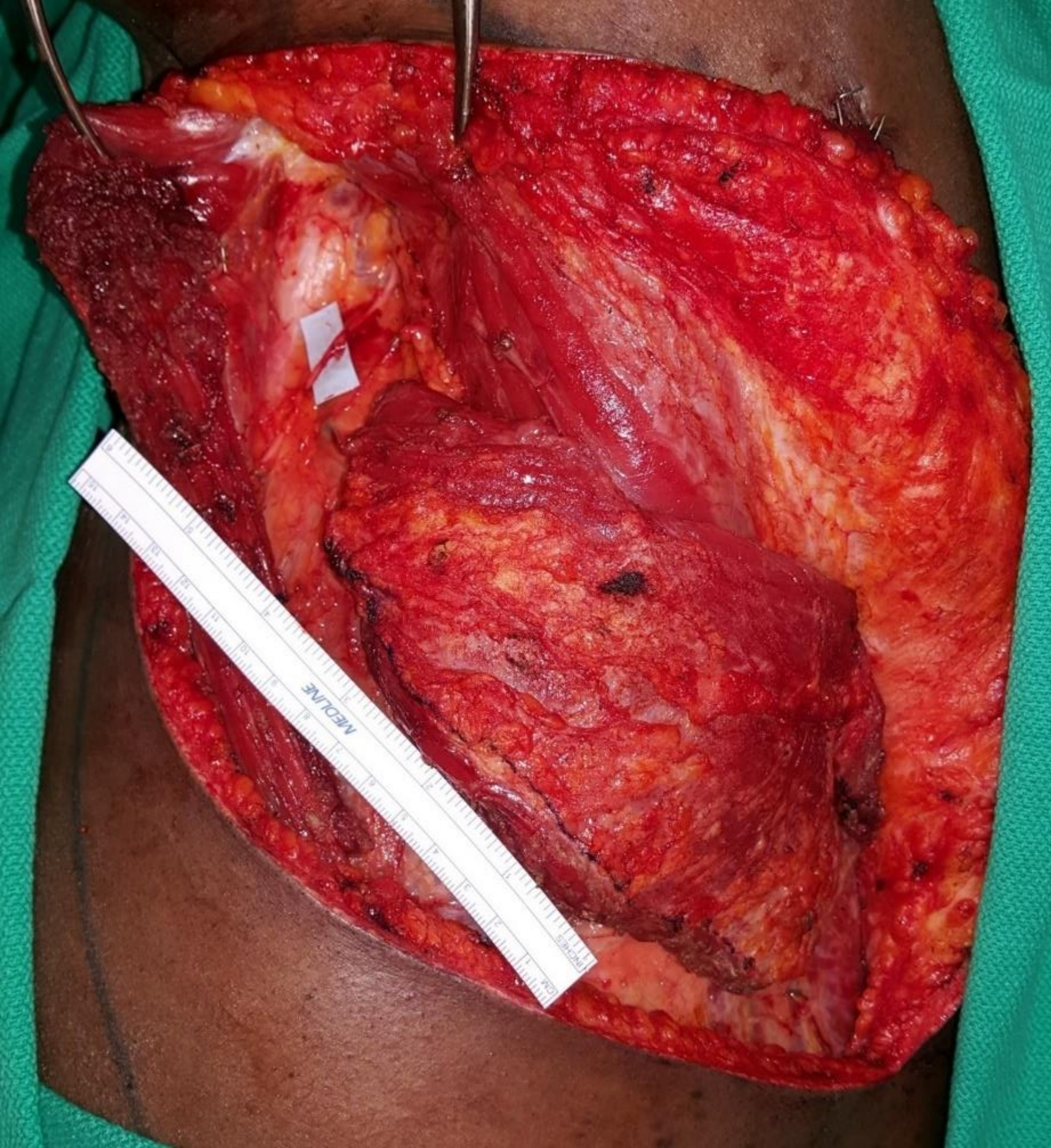
THORACODORSAL NERVE

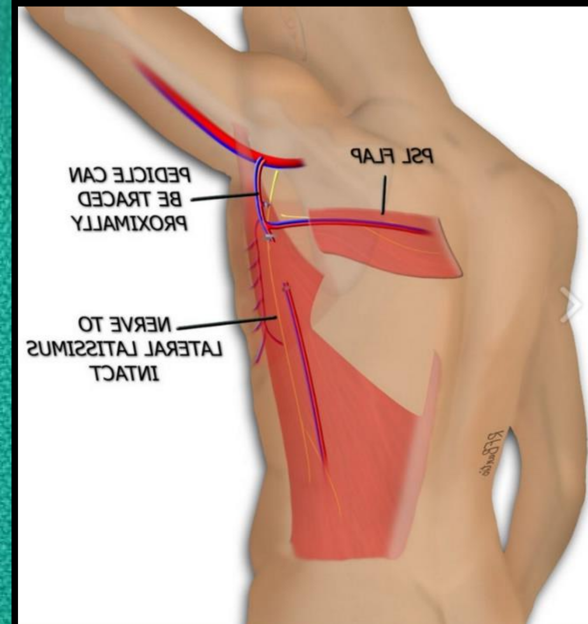
CASE 6

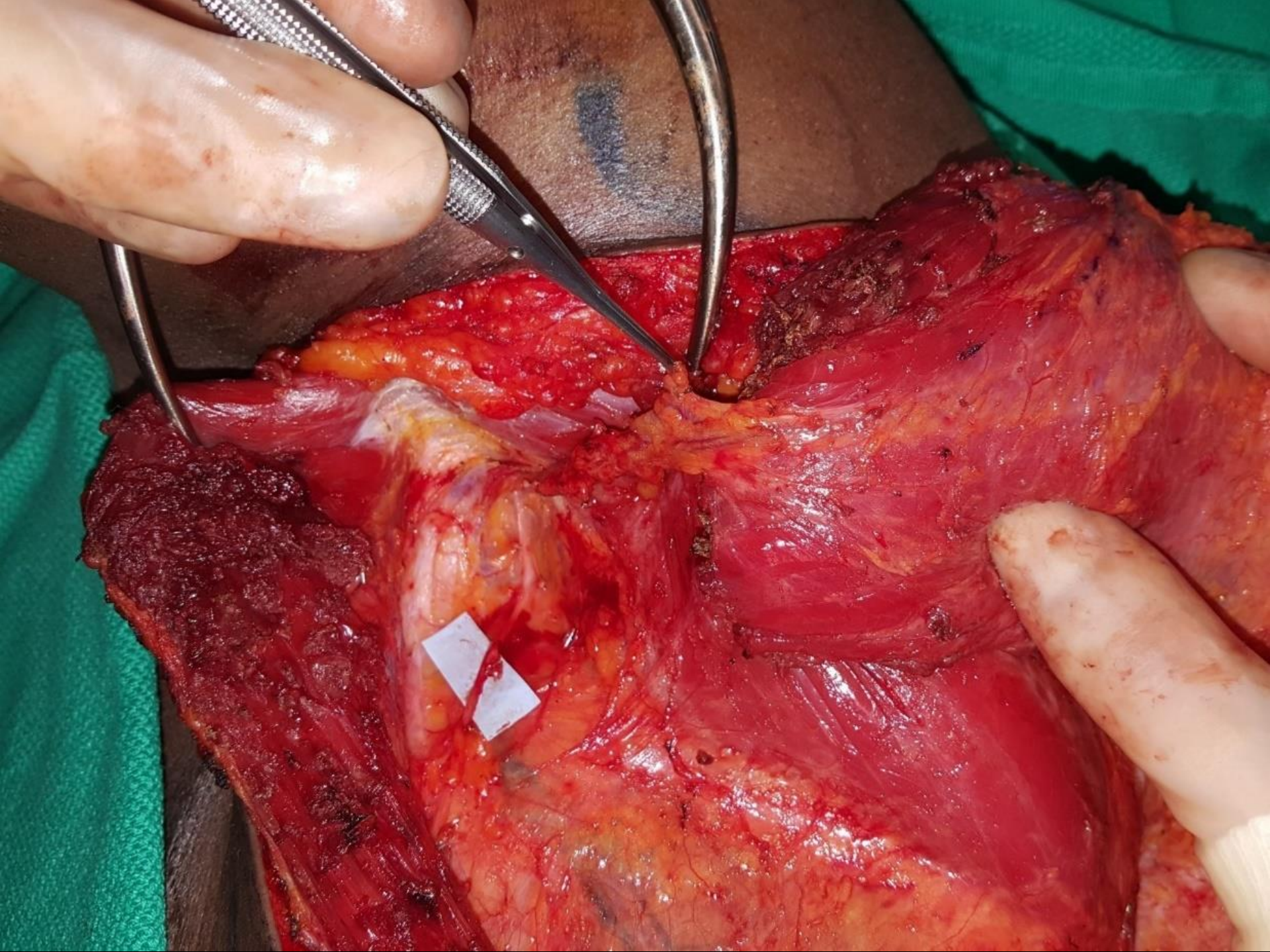

AXILLARY ARTERY
CIRCUMFLEX SCAPULAR ARTERY
SUBSCAPULAR ARTERY
THORACODORSAL ARTERY
BRANCH TO SERRATUS
LATISSIMUS
PSL FLAP

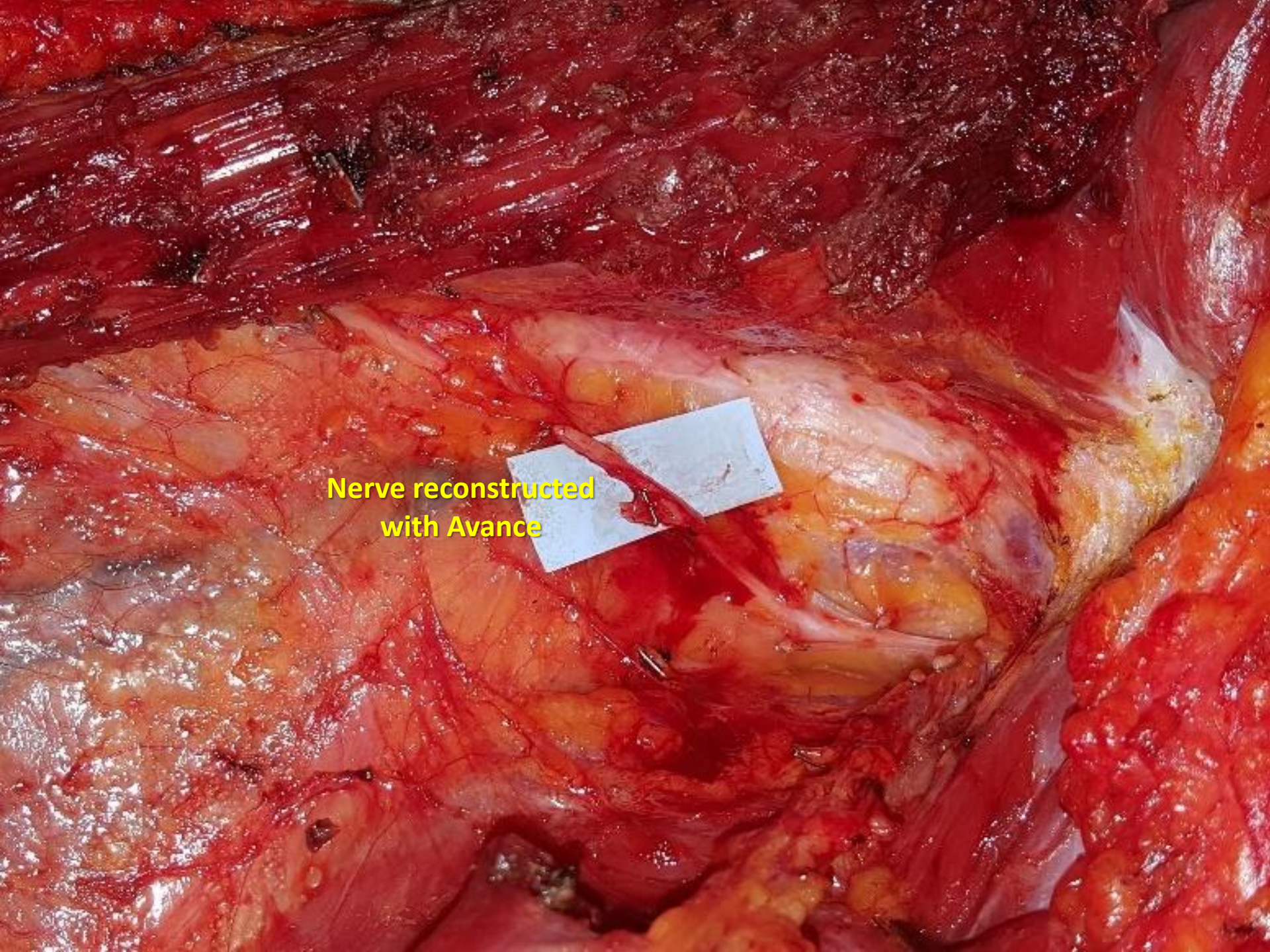

PSL FLAP
PEDICLE CAN BE TRACED PROXIMALLY
NERVE TO LATERAL LATISSIMUS INTACT
R.F.Bartis

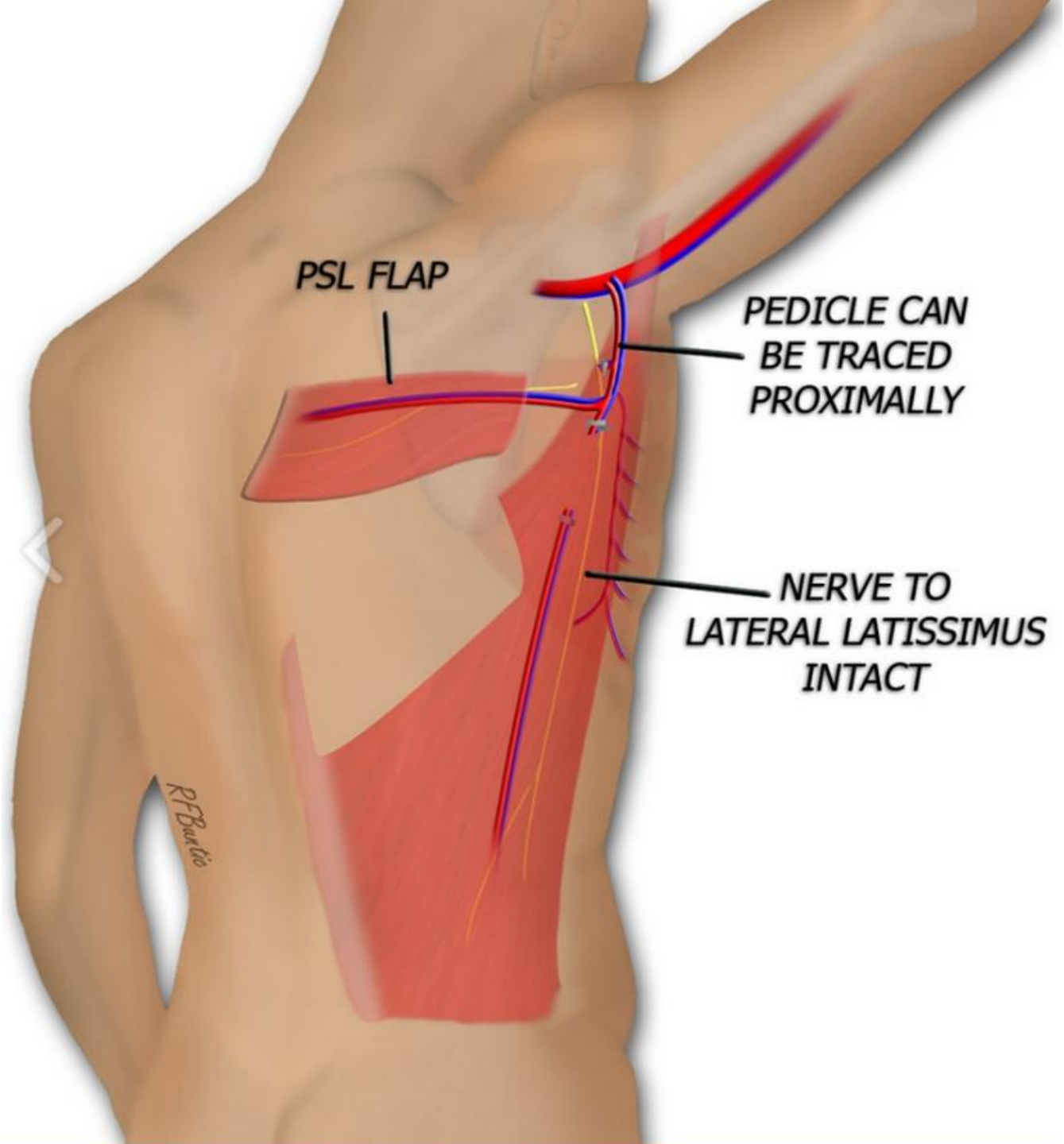



MEDLINE


PSL FLAP
PEDICLE CAN
BE TRACED
PROXIMALLY
NERVE TO
LATERAL LATISSIMUS
INTACT




Nerve reconstructed
with Avance


PSL FLAP
PEDICLE CAN BE TRACED PROXIMALLY
NERVE TO LATERAL LATISSIMUS INTACT
RFBurtie

Allograft Nerve Reconstruction Clinical Data Overview

Bauback Safa, MD, MBA, FACS,

The Buncke Clinic

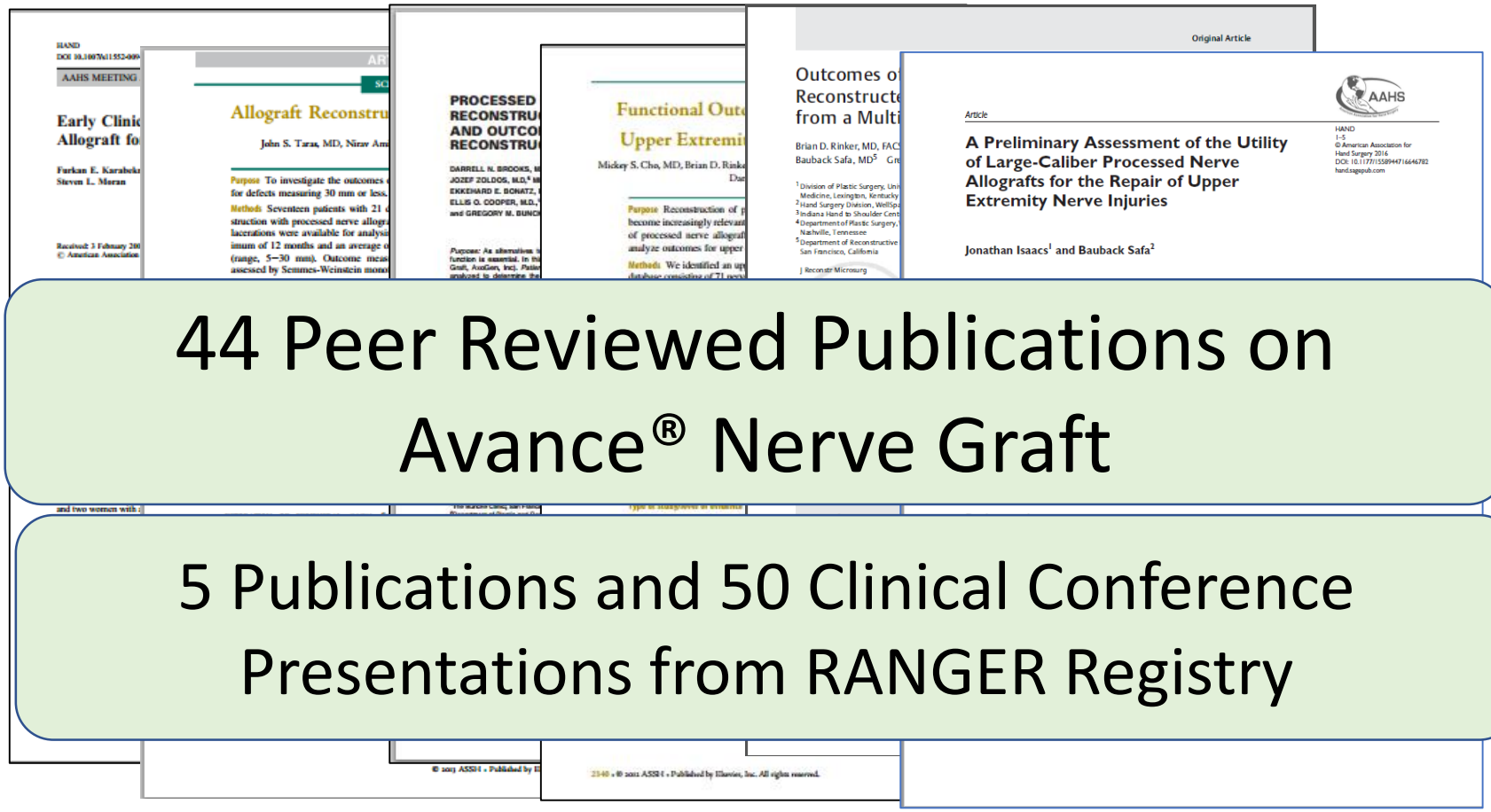
Assistant Clinical Professor, Stanford Plastic Surgery

Assistant Clinical Professor, UCSF Plastic Surgery

Stanford MEDICINE

T B C SINCE 1970

UCSF University of California San Francisco



44 Peer Reviewed Publications on Avance® Nerve Graft

5 Publications and 50 Clinical Conference Presentations from RANGER Registry

- Largest multi-center clinical study in peripheral nerve repair (>1000 nerve repairs!)
  - Processed Nerve Allograft
  - Contemporary Controls (MATCH Study Arm)
    - Autograft
    - Hollow Tube Conduits
- Multicenter standardized data collection for “Real Time” tracking of:
  - Demographics, injury, and treatment
  - Quantitative and qualitative outcomes
- Data management and analysis conducted independently with pre-defined criteria

Actively Enrolling RANGER Sites

Institution	Principal Investigator
The Buncke Clinic	Greg Buncke, MD
Johns Hopkins	John Ingari, MD
Duke University	Fraser Leversedge, MD
San Antonio MMC	Mickey Cho, MD
Univ of Kentucky	Brian Rinker, MD
Multi-Disciplinary Specialties	Renata Weber, MD
Cleveland Clinic	Steven Maschke, MD
Vanderbilt University	Wesley Thayer, MD Mihir Desai, MD
University of Cincinnati	David McGee MD

Institution	Principal Investigator
Walter Reed NMMC	Patricia McKay, MD
MetroHealth	Harry Hoyen, MD
John Peter Smith UNTHSC	Timothy Niacarus, MD
Phoenix Children's Hosp	P. David Adelson, MD
Ohio State Univ.	Sonu Jain, MD
Arizona Center for Hand Surgery	Josef Zoldos, MD
Univ of Washington	Jeffrey Friedrich, MD
Children's Hosp of Atlanta	Bryce Gillespie, MD
Florida Orthopaedic Institute	Jason Nydick, MD
York Hospital, Toronto	Yasser El-Sheikh MD

Outcome Reporting from RANGER

Medical Research Council Classification (MRCC) of Sensory Recovery as modified by Mackinnon		Medical Research Council Classification (MRCC) of Motor Recovery as modified by Mackinnon	
S0	Absence of sensibility in the autonomous area	M0	No contraction
S1	Recovery of deep cutaneous pain sensibility within the autonomous area of the nerve	M1	Return of perceptible contraction in the proximal muscles
S2	Return of some degree of superficial cutaneous pain and tactile sensibility within the autonomous area of the nerve	M2	Return of perceptible contraction in both proximal and distal muscles
S3	Return of superficial cutaneous pain and tactile sensibility throughout the autonomous area, with disappearance of any previous over response	M3	Return of function in both proximal and distal muscles to such a degree that all important muscles are sufficiently powerful to act against gravity
S3+	Return of sensibility as in S3; in addition, there is some recovery of 2-point discrimination within the autonomous area (7-15 mm)	M4	All muscles act against strong resistance and some independent movements are possible
S4	Complete recovery (2-point discrimination, 2-6 mm)	M5	Full recovery in all muscles

Meaningful Recovery

Higher Threshold of Recovery

Widely Accepted Convention:
Allografts Work for Sensory Gaps

	N	Gap (mm)	m2PD	s2PD	% MR (S3/S4)	% HT MR (S3+/S4)
Moran 2009	10	22.3 (5-30)	4.4	5.5	100%	100%
Brooks 2011	49	19 ± 8	8	8	89.5%	NR
Cho 2012	44	22 (5-50)	8	8	86%	NR
Taras 2013	18	11 (5-30)	NR	7	100%	100%
Rinker 2015	37	11 ± 3	NR	7.1	92%	84%
Zuniga 2014	23	34 (8-70)	NR	NR	87%	NR
Means 2016	7	12 (5-20)	5	5	100%	100%
Rinker 2017	50	35 (27-50)	NR	9	86%	64%

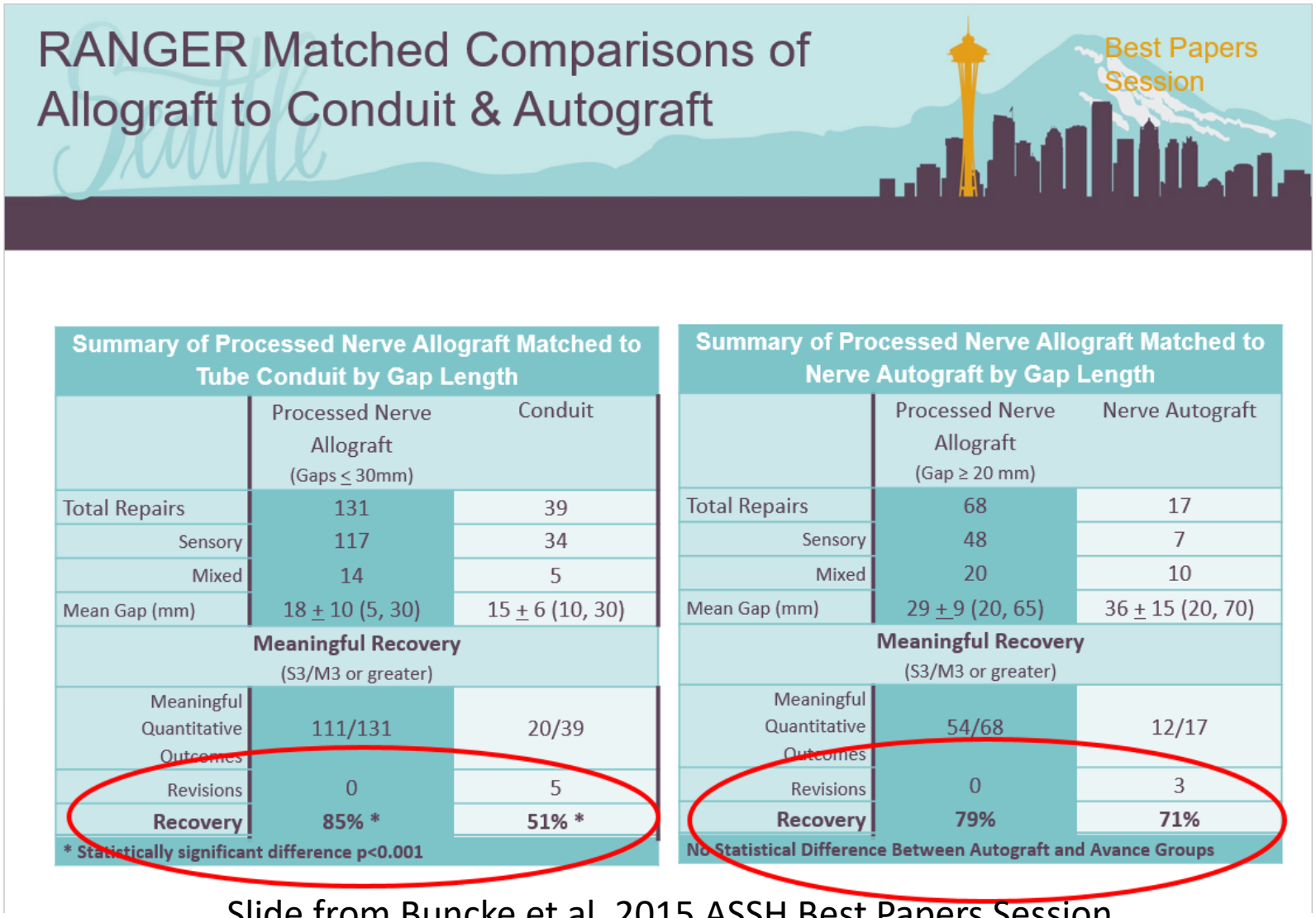
HISTORICAL CONTROLS:

Conduit : 40-72%

Autograft: 60-88%

MATCH Study

A Comparison of Peripheral Nerve Allograft to Contemporary Controls



Summary of Processed Nerve Allograft Matched to Tube Conduit by Gap Length

	Processed Nerve Allograft (Gaps ≤ 30mm)	Conduit
Total Repairs	131	39
Sensory	117	34
Mixed	14	5
Mean Gap (mm)	18 ± 10 (5, 30)	15 ± 6 (10, 30)
Meaningful Recovery (S3/M3 or greater)		
Meaningful Quantitative Outcomes	111/131	20/39
Revisions	0	5
Recovery	**85% ***	**51% ***

*** Statistically significant difference p<0.001**

Summary of Processed Nerve Allograft Matched to Nerve Autograft by Gap Length

	Processed Nerve Allograft (Gap ≥ 20 mm)	Nerve Autograft
Total Repairs	68	17
Sensory	48	7
Mixed	20	10
Mean Gap (mm)	29 ± 9 (20, 65)	36 ± 15 (20, 70)
Meaningful Recovery (S3/M3 or greater)		
Meaningful Quantitative Outcomes	54/68	12/17
Revisions	0	3
Recovery	**79%**	**71%**

No Statistical Difference Between Autograft and Avance Groups

Slide from Buncke et al. 2015 ASSH Best Papers Session.

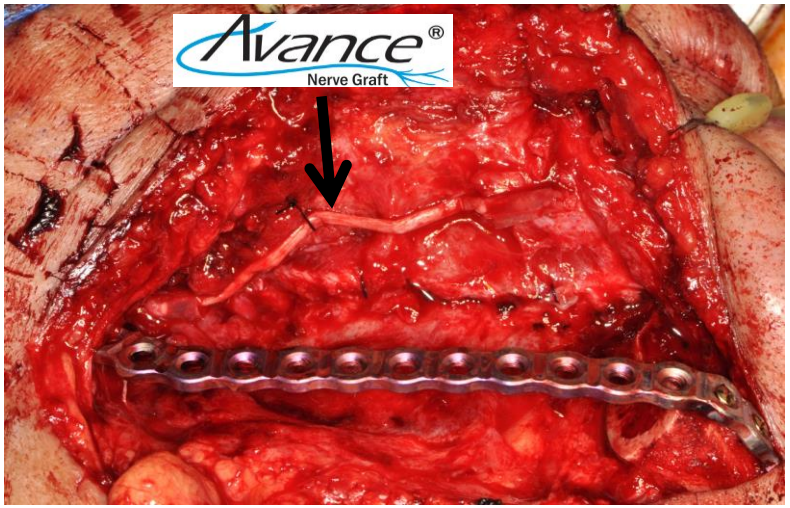
Do Allografts Work in Long Gaps?

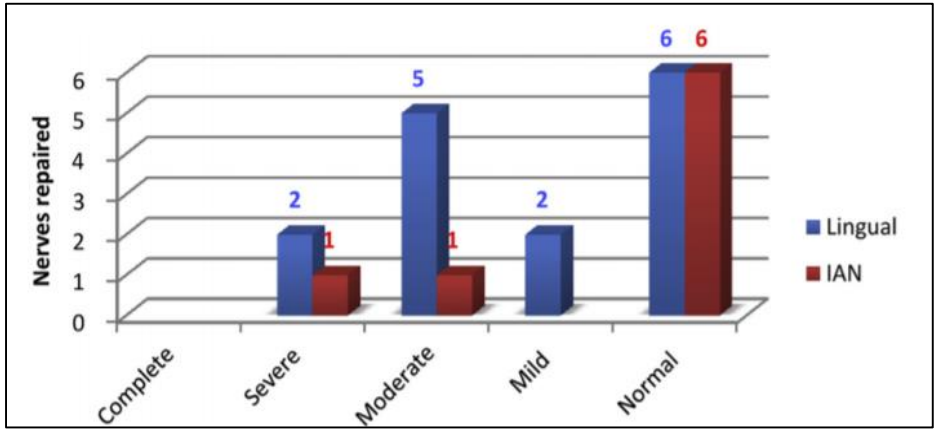
- 28 lingual and inferior alveolar nerve discontinuities
- 100% improved
- 52% recovered to normal sensation

SURGICAL ONCOLOGY AND RECONSTRUCTION

Sensory Outcomes After Reconstruction of Lingual and Inferior Alveolar Nerve Discontinuities Using Processed Nerve Allograft—A Case Series

*John R. Zuniga, DMD, MS, PhD**





Gap Length	% Showing Improvement
11-30mm	82%
31-70mm	83%

Do Allografts Work in Long Gaps?

- Rinker et al. 2017 Annals of Plastic Surgery
- Subgroup analysis from the RANGER Registry
- 50 digital nerve repairs
- Mean gap length 35 ± 8 (25, 50) mm
- Outcomes consistent across gap range
- Versus historical controls in the literature
  - Exceeds hollow tube conduit
  - Comparable to autograft

TABLE 3. Distribution of MRCC Scores for Return of Sensory Function

Sensory MRCC Score	Gaps 26–39 mm	Gaps 40–50 mm	Cumulative Group
S0	2	2	4
S1	1	0	1
S2	1	0	1
S3	11	1	12
S3+	18	10	28
S4	3	1	4
MRCC ≥ S3	89%	86%	86%

Do Allografts Work for Mixed and Motor Nerve Injuries?

Setting Expectations vs. Autograft, The Gold Standard

Comparison to Historical Reference Literature				
Study	**Nerve Injury Types**	**Test Article**	**Level of Recovery**	**Positive Outcomes***
Nerve Autograft Studies				
Weber, et al., 2000	Sensory Nerves	Direct Repair and Autograft	**≥S3**	**86%**
Kim and Kline 2001-2006	Sensory and Mixed Nerves	Direct Suture and Autograft	**≥S3/M3**	**67-%**
Frykman and Gramyk, 1991	Sensory Nerves	Autograft for Digital Nerve Injury under 5 cm	**≥S3**	**70%**
Frykman and Gramyk, 1991	Mixed Nerves	Direct Suture and Autograft	**≥S3/M3**	**70-75%**
Kallio, et al., 1993	Sensory Nerves	Autograft and Direct Repair	**≥S3/M3**	**67%**
Matejcik et al. 2003	Sensory and Mixed Nerves	Autograft	**≥S3/M3**	**60-80%**
Donzelli et al. 1998	Sensory Nerves and Mixed Nervs	Autrograft	**≥S3/M3**	**65%**
Rjuis et al. 2005	Mixed Nerves	Autograft	**≥S3+/M4**	**51%**

* As reported, based on individual study parameters for acceptable recovery: M3-M5, S3-S4 by MRCC

RANGER Mixed & Motor Subgroup Analysis: Inclusion Criteria

- Upper extremity and head and neck mixed and motor nerve repairs
- Minimum of 6 months follow up
- Reported relevant assessments sufficient for outcome evaluation using the Medical Research Council (MRC) scale for motor function

Relevant Assessments for Specific Nerve Repairs

Nerve Repaired	Functional Assessment
Median nerve, forearm	Flexion of the thumb, index and middle fingers as well as the ability to form a composite fist
Median nerve, wrist	Palmar abduction of the thumb; flexion of the index and middle fingers at metacarpophalangeal joints
Radial nerve, upper arm	Extension of the wrist; abduction of the wrist
Radial nerve, forearm	Supination of the forearm
Ulnar nerve, forearm	Flexion of the ring and small fingers at distal interphalangeal joints
Ulnar nerve, wrist	Key pinch; abduction of small finger; flexion of ring and small fingers at metacarpophalangeal joints
Musculocutaneous nerve, biceps branch	Elbow flexion
Spinal accessory nerve	Shoulder elevation
Facial nerve, buccal, mandibular and zygomatic branches	Lip movement (whistling, smiling, puckering and pouting the lip)

Overall Summary of Outcomes

- No significant difference was found in subject age, pre-operative interval or follow-up length among subgroups
- Meaningful recovery was reported in 75% of mixed and motor nerve repairs overall
- No related adverse events reported
- No significant difference in MR between:
  - Mechanism of injury
  - Gap length

	All	Gap Length (mm)		
		10-25	26-49	≥50
No. of Repairs	36	16	13	7
Age (years)	39 ± 19	41 ± 20	44 ± 20	28 ± 9
Pre-op Interval (days)[a]	8.5 (0, 133)	7.5 (0, 96)	5 (0, 133)	45 (9, 125)
Follow-up Duration (days)	594 ± 441	619 ± 347	506 ± 314	698 ± 719
Mechanism of Injury[b]				
Laceration	19	11	6	2
Complex	13	3	5	5
Surgical resection	4	2	2	0
Meaningful Recovery (MR)	27	11	10	6
%MR	75%	69%	77%	86%

Summary of Outcomes by Nerve

Nerve	No. of Repairs	Gap (mm)	MR	%MR
Median	18	35 ± 21	15	83%
Ulnar	10	33 ± 21	4	40%
Radial	3	48 ± 14	3	100%
Musculocutaneous	1	15 ± 0	1	100%
Spinal Accessory	1	12 ± 0	1	100%
Facial	3	27 ± 2	3	100%
All	36	34 ± 20	27	75%

Significant Difference (p=0.03)

Summary of RANGER Mixed and Motor Subgroup Analysis

- Processed nerve allografts provided functional motor recovery for mixed and motor nerve repairs in the upper extremity
- Subgroup analysis showed no differences between gap lengths or mechanism of injury
- Median nerve repairs showed a higher rate of meaningful recovery than ulnar nerve repairs and was comparable to historical controls for nerve autograft
- Outcomes compare favorably to historical controls from available literature for nerve autograft and exceed that of nerve conduit
- The overall success rate and safety supports the use of processed nerve allograft within the treatment algorithms for mixed and motor nerve injuries
- The RANGER® registry is currently ongoing and future reports from it will provide additional clinical evidence on the expanding role of PNA in mixed and motor nerve repairs