Trial of Ultrasound guided carpal tunnel release versus Traditional Open Release (TUTOR)

Kyle R. Eberlin
Massachusetts General Hospital

Christopher J. Dy
Washington University School of Medicine in St. Louis

Mark D. Fischer
Twin Cities Orthopedics

James L. Gluck
Kansas Orthopaedic Center

F. Thomas D. Kaplan
Indiana Hand to Shoulder

See next page for additional authors

Follow this and additional works at: https://digitalcommons.wustl.edu/oa_4

Recommended Citation
https://digitalcommons.wustl.edu/oa_4/674

This Open Access Publication is brought to you for free and open access by the Open Access Publications at Digital Commons@Becker. It has been accepted for inclusion in 2020-Current year OA Pubs by an authorized administrator of Digital Commons@Becker. For more information, please contact vanam@wustl.edu.
Trial of ultrasound guided carpal tunnel release versus traditional open release (TUTOR)

Kyle R. Eberlin, MD, Christopher J. Dy, MD, MPH, Mark D. Fischer, MD, James L. Gluck, MD, F. Thomas D. Kaplan, MD, Thomas J. McDonald, MD, Larry E. Miller, PhD, PStat, Alexander Palmer, DO, Marc E. Walker, MD, MBA, James F. Watt, DO

Abstract

Background: Carpal tunnel release (CTR) is a surgical treatment option for patients with carpal tunnel syndrome (CTS) symptoms that are unresponsive to conservative treatment. Most patients experience symptomatic relief after CTR regardless of the surgical technique. However, direct comparisons of the safety and effectiveness between CTR surgical techniques are limited. The purpose of this randomized controlled trial is to compare the safety and effectiveness of CTR with ultrasound guidance (CTR-US) versus mini-open CTR (mOCTR) in subjects with symptomatic CTS.

Design and methods: TUTOR (Trial of Ultrasound guided CTR versus Traditional Open Release) is a randomized controlled trial in which 120 subjects at up to 12 sites in the United States will be randomized (2:1) to receive CTR-US or mOCTR. The primary endpoint of the study is the percentage of patients who return to normal daily activities within 3 days of the procedure. Secondary endpoints of the study are median time to return to normal daily activities, percentage of patients who return to work within 3 days of the procedure, median time to return to work, Boston Carpal Tunnel Questionnaire Symptom Severity Scale (BCTQ-SSS) change score at 3 months, BCTQ Functional Status Scale (BCTQ-FSS) change score at 3 months, Numeric Pain Scale change score at 3 months, EuroQoL-5 Dimension 5-Level (EQ-5D-5L) change score at 3 months, and the incidence of device- or procedure-related adverse events at 3 months. Patient follow-up in this trial will continue for 1 year.

Ethics and dissemination: This study was approved by a central institutional review board and ongoing trial oversight will be provided by a data safety monitoring board (DSMB). The authors intend to report the results of this trial at medical conferences and peer-reviewed journals. The outcomes of TUTOR will have important clinical and economic implications for all stakeholders involved in treating patients with CTS.


Level of evidence: 1

Abbreviations: AE = adverse event, BCTQ-FSS = Boston Carpal Tunnel Questionnaire Functional Status Scale, BCTQ-SSS = Boston Carpal Tunnel Questionnaire Symptom Severity Scale, CTR = carpal tunnel release, CTR-US = carpal tunnel release with ultrasound guidance, CTS = carpal tunnel syndrome, DSMB = data safety monitoring board, EQ-5D-5L = EuroQoL-5 Dimension 5-Level, mOCTR = mini-open carpal tunnel release, OCTR = open carpal tunnel release, TCL = transverse carpal ligament, TUTOR = trial of ultrasound guided carpal tunnel release versus traditional open release.

Keywords: carpal tunnel release, carpal tunnel syndrome, randomized controlled trial, TUTOR, ultrasound.

1. Introduction

Carpal tunnel syndrome (CTS) is the most common peripheral compression neuropathy, affecting approximately 5% of the population.[1] A multitude of treatments are available to treat CTS including activity modification, bracing/splinting, hand therapy, modalities (e.g., therapeutic lasers or ultrasound, iontophoresis), acupuncture, corticosteroid injections, and carpal tunnel release (CTR) surgery.[2–7] Currently, there is no universally accepted algorithm to guide treatment for patients suffering from CTS. The American Academy of Orthopedic Surgery CTS Clinical Practice Guidelines reported that only 3 treatments are strongly supported in the literature: splinting, corticosteroid injections, and CTR.[8] Although some patients...
with mild to moderate symptoms are successfully treated with splinting and/or corticosteroid injections, those with progressive, refractory, or severe symptoms often undergo CTR for definitive management.\textsuperscript{[2,3,5-8]}

The goal of CTR is to reduce pressure on the median nerve by dividing the transverse carpal ligament (TCL) while avoiding iatrogenic injury to surrounding neurovascular structures. Among approximately 600,000 CTR procedures performed in the United States annually,\textsuperscript{[1,10]} most (70\%–80\%) use an open technique (OCTR) during which a palmar incision is made to dissect down to the TCL and transect it using a scalpel, scissors, or a similar cutting device.\textsuperscript{[11-13]} The standard OCTR technique requires a relatively large incision of 3 to 5 cm and may be associated with a prolonged recovery period due to palmar pain and the need to protect the wound.\textsuperscript{[12,14-17]}

Over time, there has been a trend to use smaller incisions (1–3 cm) to reduce surgical morbidity using mini-OCTR (mOCTR) or endoscopic CTR.\textsuperscript{[11,16-18]} Because long-term outcomes and complication profiles are generally equivalent among these CTR procedures,\textsuperscript{[19]} factors related to patient recovery time such as time to return to normal activities and work absenteeism are important considerations that may assist in shared treatment decision-making between physicians and patients.

In recent years, multiple studies have demonstrated the feasibility of using ultrasound to perform CTR through even smaller incisions while maintaining or improving visualization of the carpal tunnel region, including its at-risk neurovascular structures. During CTR using ultrasound guidance (CTR-US), the carpal tunnel is typically accessed through a single small wrist or palmar incision less than 5 mm length and the TCL is transected using a small knife or similar cutting instrument while the carpal tunnel structures are monitored using ultrasound during the procedure. To date, 13 clinical studies have been published reporting results on over 1300 hands in over 1000 patients at up to 2 years post-treatment comparing recovery time, effectiveness, and safety in subjects with CTS treated with CTR-US or mOCTR.\textsuperscript{[20-32]} Among these over 1300 hands, there were no major neurovascular complications, and the clinical success rate was over 95\%. Furthermore, 2 randomized controlled trials and 1 prospective non-randomized trial demonstrated superior early outcomes for CTR-US compared to mOCTR.\textsuperscript{[22,23,29]} However, these trials have been limited by small sample size, short follow-up duration, or both. No randomized controlled trial comparing CTR-US to mOCTR has been performed with a sample size over 100 patients and with at least 1 year of follow-up. Thus, the objective of this randomized controlled trial is to compare the safety and effectiveness of CTR-US versus mOCTR in a large cohort of subjects (n = 120) with symptomatic CTS followed for 1 year post-treatment.

2. Design and Methods

This paper describes the rationale and design of TUTOR (Trial of Ultrasound guided CTR versus Traditional Open Release). The protocol was developed in accordance with the SPIRIT 2013 guidance for protocols of clinical trials.\textsuperscript{[33]}

2.1. Study design

This is a prospective, multicenter, randomized controlled trial that will be performed at up to 12 sites in the United States. Subject recruitment in the study began July 26, 2022. A total of 120 subjects will be enrolled and randomized (2:1) to receive CTR-US or mOCTR. The total study duration is expected to be approximately 1.5 years, with 6 months of anticipated subject recruitment and 1 year of follow-up. The trial was prospectively registered at ClinicalTrials.gov (NCT05405218) before first subject enrollment. The trial was funded by Sonex Health, Inc. (Eagan, MN) who was involved in trial design, but will not be involved in data analysis or publication of trial results. Ongoing trial oversight will be provided by a data safety monitoring board (DSMB) and data will be routinely monitored for accuracy. A list of investigational sites and trial oversight committees is provided in Table 1.

2.2. Participants and eligibility criteria

Study participants will undergo a preoperative clinical examination and diagnostic ultrasound of the median nerve. Key eligibility criteria of the trial are a clinical diagnosis of unilateral or bilateral idiopathic CTS, a score of 12 or greater on the CTS-6 questionnaire in the target hand,\textsuperscript{[4]} median nerve cross-sectional area \textgreater 10 mm\textsuperscript{2} in the proximal carpal tunnel region of the target hand,\textsuperscript{[4]} absence of carpal tunnel symptoms in the contralateral hand that interfere with work or daily activities, and prior failure of nonsurgical CTS treatment. Key exclusion criteria are previous surgery on the target hand or wrist, recent (<6 weeks) corticosteroid injection in the target hand or wrist, need for additional operative procedure, and planned surgical or interventional procedure on the contralateral wrist or hand. Subjects

Table 1

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution *</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kyle R. Eberlin, MD **</td>
<td>Massachusetts General Hospital</td>
<td>Boston, MA</td>
</tr>
<tr>
<td>Christopher J. Dy, MD, MPH, FACS</td>
<td>Washington University</td>
<td>St. Louis, MO</td>
</tr>
<tr>
<td>James F. Watt, MD</td>
<td>Orthopedic Associates</td>
<td>Fort Walton, FL</td>
</tr>
<tr>
<td>James L. Gluck, MD</td>
<td>Kansas Orthopaedic Center</td>
<td>Wichita, KS</td>
</tr>
<tr>
<td>Alexander Palmier, DO</td>
<td>Sano Orthopedics</td>
<td>Lee’s Summit, MO</td>
</tr>
<tr>
<td>F. Thomas D. Kaplan, MD, FAAOS</td>
<td>Indiana Hand to Shoulder</td>
<td>Indianapolis, IN</td>
</tr>
<tr>
<td>Thomas J. McDonald, MD</td>
<td>Sierra Orthopedic Institute</td>
<td>Sonora, CA</td>
</tr>
<tr>
<td>Mark D. Fischer, MD</td>
<td>Twin Cities Orthopedics</td>
<td>Maple Grove, MN</td>
</tr>
<tr>
<td>Marc E. Walker, MD, MBA</td>
<td>University of Mississippi Medical Center</td>
<td>Jackson, MS</td>
</tr>
</tbody>
</table>

Data safety monitoring board

Kevin C. Chung, MD, MS
Julie E. Adams, MD
Warren C. Hammert, DDS, MD

Independent medical reviewer

Kevin C. Chung, MD, MS

TUTOR = Trial of Ultrasound guided carpal tunnel release versus Traditional Open Release

*Up to 12 investigational sites may participate in this study. The list of sites in the table represents those that were active as of September 12, 2022.

**Study principal investigator.
who meet all preoperative eligibility criteria will be randomized
to receive CTR-US or mOCTR. A complete list of study eligibil-
ity criteria is provided in Table 2.

2.3. Randomization

The randomization sequence for this trial was developed by
an independent biostatistician and computer-generated by an
electronic data capture system (Viedoc, Philadelphia, PA). A
2:1 (CTR-US: mOCTR) randomization ratio will be utilized
with the randomization sequence stratified by site using vari-
able block sizes to minimize treatment allocation predictability.
Treatment assignment will be concealed until it is presented to
authorized site personnel at the time of randomization.

2.4. Blinding

Because of obvious differences in surgical technique, it is
not possible to blind the treating physicians. As the result of
notable visual differences in the postoperative scar between
surgical techniques (~3–5 mm for CTR-US and ~1–3 cm for
mOCTR), it is not possible to blind the subjects. Due to the
fact that the majority of data collected in this trial will be
subject-reported, it is not feasible to blind outcome assessors
(i.e., subjects).

2.5. Surgical procedure

Subjects randomized to CTR-US will be treated with the com-
mercially available UltraGuideCTR (Sonex Health, Inc., Eagan,
MN). The device is a single-use, hand-held device that is inserted
into the carpal tunnel through a small (typically < 5 mm) inci-
sion at the proximal wrist using real-time ultrasound guidance.
The working tip of the UltraGuideCTR consists of 2 inflatable
balloons that border a centrally located, retractable retrograde
cutting blade. Ultrasound is used to position the tip inferior and
distal to the TCL and the balloons are inflated with sterile saline,
increasing the tip diameter to 8 mm. The inflated balloons dis-
place the median nerve and ulnar artery away from the device,
with safe position verified with ultrasound. The blade is then
activated, and the TCL is transected in a retrograde manner,
with ultrasound visualizing the transection and verifying safe
position of the neurovascular structures. Following TCL tran-
section, the blade is recessed, the balloons are deflated, and the
device is removed. The TCL is then probed to ensure a complete
release. In subjects randomized to mOCTR, the TCL will be
divided through a 1 to 3 cm incision in standard fashion with-
out ultrasound guidance. Postoperative patient care instructions
will be standardized for each treatment group and among all
participating sites in order to minimize bias. Investigators will
instruct subjects to participate in activities and return to work,
as tolerated, based on pain, function, and wound healing status.

2.6. Outcomes

Subject data will be recorded using electronic case report
forms and will be routinely monitored for accuracy. Follow-up
assessments will occur daily for the first 14 post-proce-
dure days, and at 4 weeks, 3 months, 6 months, and 1 year
post-treatment thereafter. Time to return to normal activi-
ties and return to work will be assessed daily. Boston Carpal
Tunnel Questionnaire Symptom Severity Scale (BCTQ-SSS)
and Functional Status Scale (BCTQ-FSS), Numeric Pain Scale,
EuroQoL-5 Dimension 5-Level (EQ-5D-5L), and adverse
events (AEs) will be assessed at each follow-up interval. A
schedule of subject assessments during the study is provided in
Table 3.

Table 2

Subject eligibility criteria.

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. ≥18 yrs of age</td>
</tr>
<tr>
<td>2. Clinical diagnosis of unilateral or bilateral idiopathic CTS</td>
</tr>
<tr>
<td>3. CTS-6 score &gt;12 in target hand</td>
</tr>
<tr>
<td>4. Absence of carpal tunnel symptoms in the contralateral hand that interfere with normal daily activities or work at the time of consent and are not anticipated to interfere with return to activities or return to work within at least 3 mo post-operatively</td>
</tr>
<tr>
<td>5. Median nerve cross-sectional area ≥10 mm² in the proximal carpal tunnel region of the target hand measured by diagnostic ultrasound</td>
</tr>
<tr>
<td>6. Prior failure of one or more nonsurgical treatment options for the target hand (e.g., physical activity modification, bracing, splinting, corticosteroid injection)</td>
</tr>
<tr>
<td>7. Subject agrees to complete follow-up questionnaires over a 12-mo period</td>
</tr>
<tr>
<td>8. Subject has a valid mobile phone number and email address to receive and answer follow-up questionnaires</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Prior surgery on the target wrist or hand with the exception of trigger finger that has clinically recovered</td>
</tr>
<tr>
<td>2. History of prior surgical CTR in the target hand</td>
</tr>
<tr>
<td>3. History of prior surgical CTR in the contralateral hand within 3 mo of enrollment or with persistent symptoms that interfere with normal daily activities or work at the time of consent</td>
</tr>
<tr>
<td>4. Corticosteroid injection in the target wrist or hand within 6 wks of randomization</td>
</tr>
<tr>
<td>5. Presence of additional process in the target wrist or hand requiring additional intervention beyond carpal tunnel release (e.g., neurolysis, mass removal, tenosynovectomy)</td>
</tr>
<tr>
<td>6. Clinically significant degenerative arthritis of the upper limb (shoulder to hand) on the target side</td>
</tr>
<tr>
<td>7. Clinically significant inflammatory disease (including tenosynovitis) of the upper limb (shoulder to hand) on the target side</td>
</tr>
<tr>
<td>8. Clinically significant trauma or deformity of the upper limb (shoulder to hand) on the target side</td>
</tr>
<tr>
<td>9. Clinically significant vascular disease (including Raynaud’s phenomenon) of the upper limb (shoulder to hand) on the target side</td>
</tr>
<tr>
<td>10. Clinically significant neurological disorder (including complex regional pain syndrome) of the upper limb (shoulder to hand) on the target side</td>
</tr>
<tr>
<td>11. Planned surgical or interventional procedure on the contralateral wrist or hand</td>
</tr>
<tr>
<td>12. Systemic inflammatory disease (e.g., rheumatoid arthritis, lupus)</td>
</tr>
<tr>
<td>13. Amyloidosis</td>
</tr>
<tr>
<td>14. Chronic renal insufficiency requiring dialysis</td>
</tr>
<tr>
<td>15. Diabetes not controlled by a stable dose of medication over the past 3 mo</td>
</tr>
<tr>
<td>16. Uncontrolled thyroid disease</td>
</tr>
<tr>
<td>17. Pregnant or planning pregnancy in the next 12 mo</td>
</tr>
<tr>
<td>18. Workers compensation subjects</td>
</tr>
<tr>
<td>19. Inability to provide a legally acceptable Informed Consent Form and/or comply with all follow-up requirements</td>
</tr>
<tr>
<td>20. Subject has other medical, social or psychological conditions that, in the opinion of the investigator, preclude them from receiving the pretreatment, required treatment, and post-treatment procedures and evaluations</td>
</tr>
</tbody>
</table>
The primary endpoint of the study is the percentage of patients who return to normal daily activities within 3 days of the procedure, irrespective of work status. Secondary endpoints of the study are median time to return to normal daily activities, percentage of patients who return to work within 3 days of the procedure, median time to return to work, BCTQ-SSS change score at 3 months, BCTQ-FSS change score at 3 months, Numeric Pain Scale change score at 3 months, EQ-5D-5L change score at 3 months, and the incidence of device- or procedure-related AEs at 3 months. The 3-month follow-up interval was selected for analysis of secondary endpoints because the majority of clinical improvement after CTR occurs in the first 3 months, with marginal improvement thereafter.[35,36]

Among study subjects who report full-time or part-time employment preoperatively, time to return to work is defined as the number of days between treatment and the time the subject reports returning to work in any capacity. The BCTQ is a CTS-specific questionnaire that is highly reproducible, internally consistent, valid, and responsive to clinical change in CTS and subject status post-CTR.[37] The BCTQ consists of 11 symptom severity questions (BCTQ-SSS) that are scored from 1 to 5, with higher scores indicating more severe symptoms, and is calculated as the mean of each response. The BCTQ additionally consists of 8 functional status questions that are scored from 1 to 5, with higher scores indicating more functional limitation, and is calculated as the mean of each response. Subjects will be asked to rate their wrist pain severity on a Numeric Pain Scale ranging from 0 to 10, with 0 representing “no pain” and 10 representing “the worst pain imaginable.” The EQ-5D-5L is a generic preference-based questionnaire that measures quality of life across 5 domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension is scored on a 5-level severity ranking consisting of: no problems, slight problems, moderate problems, severe problems, unable to/extreme problems.[38]

Subject safety will be assessed by recording AEs. An AE is defined as any adverse change (i.e., de novo or preexisting condition) from the subject’s baseline medical condition occurring after the initial procedural incision has been initiated. Determination of whether a subject experienced an AE can be made in 3 different ways. First, an AE can be documented by the site during the study procedure. Second, a subject may report a postoperative AE directly via phone call to the investigative site. Third, an AE can be identified by the site during the review of the subject-uploaded wound healing images. If the site identifies a potential AE based on image review or is notified of a potential AE by the subject, confirmation of the AE will occur by a phone call with the subject or, if necessary, by asking the subject to return for a follow-up clinical evaluation.

Adverse events will be classified by seriousness and relationship to the device or procedure. A serious adverse event is defined as one that suggests a significant hazard or side effect, regardless of the relationship to the device or procedure. This includes, but may not be limited to, any event that results in death; is life threatening or places the participant at immediate risk of death from the event as it occurred; requires or prolongs hospitalization; causes persistent or significant disability or incapacity; results in congenital anomalies or birth defects; or is another condition which investigators judge to represent significant hazards. A device-related AE is directly attributable to the device or procedure, irrespective of work status. A procedure-related AE is directly attributable to the procedure, irrespective of the device, including complications from anesthesia or other procedures incidental to CTR. The relationship of the AE to the device or procedure will be determined by the site investigator using the following definitions:

- **Definite:** The AE follows a reasonable temporal sequence from the time of the index procedure, which includes AEs that occur during the index procedure or during the follow-up period.
- **Probable:** The AE follows a reasonable temporal sequence from the time of the index procedure, and the possibility can be excluded that factors other than the index procedure, such as underlying disease, concomitant drugs, or concurrent treatment caused the AE.
- **Possible:** The AE follows a reasonable temporal sequence from the time of the index procedure and the possibility of
The authors intend to report the results of this trial at medical conferences and peer-reviewed journals.

### 3. Discussion

CTR is a common surgical procedure that can be performed using standard open, mini-open, limited incision, endoscopic, or ultrasound-guided techniques. The results derived from TUTOR will fill an important research gap because there is currently limited evidence directly comparing the safety and effectiveness of CTR-US and mOCTR. Major strengths of the current trial include generation of Level 1 comparative evidence, a large sample size derived from multiple investigative sites, long-term follow-up, and rigorous study oversight by an independent medical reviewer and a DSMB. The initial 3-month results of this trial, including assessment of the return to normal daily activities primary endpoint, are planned to be reported in mid-2023. The outcomes of TUTOR will have important clinical and economic implications for all stakeholders involved in treating patients with CTS.

### Acknowledgments

The authors had no writing assistance in the preparation of this manuscript.

### Author contributions

**Investigation:** Kyle R. Eberlin, Christopher J. Dy, Mark D. Fischer, James L. Gluck, F. Thomas D. Kaplan, Thomas J. McDonald, Larry E. Miller, Alexander Palmer, Marc E. Walker, James F. Watt.

**Methodology:** Kyle R. Eberlin, Christopher J. Dy, Mark D. Fischer, James L. Gluck, F. Thomas D. Kaplan, Thomas J. McDonald, Larry E. Miller, Alexander Palmer, Marc E. Walker, James F. Watt.

**Writing – review & editing:** Kyle R. Eberlin, Christopher J. Dy, Mark D. Fischer, James L. Gluck, F. Thomas D. Kaplan, Thomas J. McDonald, Larry E. Miller, Alexander Palmer, Marc E. Walker, James F. Watt.

### References


