The Utility of the Harmonic Scalpel in Selective Neck Dissection: A Prospective, Randomized Trial
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Abstract

Objectives. To determine the impact of the harmonic scalpel on intraoperative blood loss and operative time in selective neck dissection (SND) (levels I-IV) for head and neck squamous cell carcinoma (HNSCC).

Study Design. Prospective randomized controlled trial.

Setting. A single, tertiary care institution (Foothills Medical Centre) in Calgary, Alberta, Canada.

Subjects. A total of 31 patients (36 neck dissections) were prospectively enrolled between January 2009 and March 2010.

Methods. Patients were randomized to receive a neck dissection with either the harmonic scalpel or the traditional technique of using electrocautery and sharp dissection. The study included adult patients older than age 18 years diagnosed with HNSCC and who required an SND (levels I-IV). Study exclusion criteria included previous treatment for head and neck cancer and all patients unwilling or unable to provide informed consent. Primary clinical outcomes were intraoperative blood loss and operative time. Secondary outcomes included intraoperative complications and surgical drain output.

Results. Intraoperative blood loss was significantly lower in the harmonic scalpel group compared to the traditional group (158 vs 61 mL, P = .02). There was no difference in operative time (81 minutes harmonic vs 85 minutes traditional) or total drain output (at both 48 hours and 1 week) between the groups. There were no intraoperative complications reported in either group.

Conclusions. Results from this study suggest that the harmonic scalpel can reduce blood loss during SND for HNSCC. The harmonic scalpel had no impact on operative time, postoperative drain output, or complication rate.

Keywords
harmonic scalpel, selective neck dissection, head and neck squamous cell carcinoma, randomized clinical trial, health technology assessment

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Neck dissection has long been used in the treatment of head and neck squamous cell carcinoma (HNSCC) and remains a common head and neck oncologic procedure. Several studies have investigated the correlation of operative time and blood loss on clinical outcomes and complications in major head and neck surgery. A study by Farwell et al demonstrated that prolonged anesthetic time (>8 hours) was associated with increased postoperative complications. Furthermore, a study by Girod et al evaluated the impact of intraoperative blood loss and demonstrated that perioperative blood transfusion was associated with increased length of stay. New technologies focused on reducing operating time and blood loss are emerging, and early results are promising.

One promising surgical tool is the harmonic scalpel (Ethicon, Cincinnati, Ohio). This instrument uses a rapidly oscillating blade (55,500 Hz) to simultaneously cut
and coagulate in a precise and controlled manner. Avoiding application of an electrical current to the tissue has the potential to minimize damage to adjacent structures and makes this an attractive instrument for use in head and neck surgery. There have been several recent studies evaluating the harmonic scalpel in patients undergoing neck dissection. These studies have demonstrated several advantages over standard sharp dissection, including reduced intraoperative blood loss and operative time while maintaining a similar complication rate compared to standard surgical approaches. Despite consistent evidence that the harmonic scalpel improves surgical efficiency during neck dissection, there are no prospective randomized studies evaluating the isolated role of the harmonic scalpel on selective neck dissection for HNSCC.

The purpose of this study is to evaluate, using a prospective randomized design, the impact of the harmonic scalpel on blood loss and operating time in patients undergoing selective neck dissection (SND) for HNSCC. Our hypothesis is that the use of the harmonic scalpel during an SND would reduce both operative time and blood loss.

Methods
This study was a prospective randomized clinical trial (www.clinicaltrials.gov registration #NCT00875953) undertaken in a consecutive cohort of patients presenting to the senior surgeons (T.W.M., J.C.D). To be eligible, patients had to be older than 18 years of age and required an SND (levels I-IV) as part of a larger oncologic resection. Patients were excluded if there was any prior treatment for head and neck cancer or if they were unwilling or unable to give informed consent. Between January 2009 and April 2010, 31 consecutive patients presenting with a diagnosis of HNSCC were eligible for this study. Thirty-six neck dissections were performed in this patient cohort. This study was reviewed and approved by the Conjoint Health Research Ethics Board at the University of Calgary.

Subjects were assigned to either the control or experimental groups via a predetermined 6 × 6 block randomization. The control group comprised 18 neck dissections in which our standard neck dissection technique (sharp dissection augmented with bipolar and/or monopolar cautery) was used. The experimental group consisted of 18 neck dissections performed primarily using the harmonic scalpel as an adjunct to sharp dissection and cautery. Two subjects (one from each arm) were excluded from analysis and follow-up because of protocol violations. The remaining 34 neck dissections followed the full study protocol with no further exclusions, drop-outs, or protocol violations. The study flow diagram can be seen in Figure 1.

Study Protocol
All patients were operated on by 1 of 2 experienced head and neck oncologic surgeons (J.C.D., T.W.M.). Before being permitted to enroll patients to the study protocol, each surgeon was required to individually perform 10 neck dissections using the harmonic scalpel to become sufficiently proficient with using the device. Preoperative characteristics for all enrolled subjects, including age, sex, body mass index (BMI), location of the primary tumor, cancer staging (TNM), and their Charlson Comorbidity Index score, were collected at the time of their enrollment.

At the time of surgery, the patient was positioned, prepped, and draped using our standard protocol. Once the tracheostomy was performed, the SND incision was marked and then injected with 0.25% bupivacaine and 1:100,000 epinephrine. Subplatysmal skin flaps were completely raised before operating time and blood loss were recorded. The Harmonic Focus handpiece (Ethicon Endo-Surgery, Cincinnati, Ohio) was used in this study. Standard bipolar and monopolar forceps (Valleylab, Inc, Boulder, Colorado) were used in the traditional surgery patients. All other surgical instruments were similar between the 2 groups. Blood loss was measured as the combined total of the volume of drainage in the suction canister and the wet weight of the sponges used (minus the dry weight of the sponges and any irrigation used during the dissection). The procedure finish time was recorded after the neck specimen was removed and hemostasis was achieved but before skin closure. The neck dissection was always performed prior to addressing the primary tumor so as to avoid confusing blood loss from the tumor resection with neck dissection-related bleeding.
In the postoperative period, data for the secondary variables were collected at 48 hours and at 1 week. These variables included postoperative complications (Clavien complication scale), cumulative drain outputs (in milliliters), the presence or absence of abnormalities around the incision site (infection, hematoma, seroma), and hospital stay (in days). Neck drains were removed when the 24-hour drainage was less than 25 mL—all drains were left for a minimum of 72 hours, and all drains were removed prior to 1 week. Completion of the protocol occurred at the 1-month period when the presence or absence of complications and the state of the incision site were recorded at a scheduled follow-up visit. Personnel measuring the secondary outcomes were blinded to the surgical technique used.

### Statistical Analysis

The power and sample sizes were calculated based on the 2 primary outcomes of interest (blood loss, procedure time) using a 2-sample comparison of means (Stata, version 11; Stata Corp, College Station, Texas). A sensitivity analysis using our own estimates of operating room (OR) time and blood loss (based on clinical experience) as well as the data from the Kos and Engelke study was performed. The sensitivity analysis and power calculation revealed that a sample size of 17 neck dissections per arm would allow us to detect differences in procedure time greater than 34 minutes and a difference in blood loss of greater than 30 mL (power 0.9, alpha 0.01). These differences were judged to be clinically meaningful.

### Results

All patients enrolled in the study underwent a SND (levels I-IV) alone or in combination with a larger oncologic resection. Clinicopathologic characteristics of the cohort can be seen in Table 1. The groups were homogeneous for age, sex, BMI, TNM staging, and comorbidity.

### Primary Outcomes

A comparison of our primary outcomes can be seen in Table 2 and is shown graphically as box plots in Figure 2. Intraoperative blood loss was significantly lower in the experimental group than in the control group (62 mL vs 158 mL, \( P = .02 \)). The mean operative time for SND was 81 minutes (95% confidence interval [CI], 73-89) in the experimental group and 85 minutes (70-100) in the control group. The difference was not statistically significant (\( P = .5 \)).

### Secondary Outcomes

No subjects experienced any intraoperative complications (vascular, neurologic, or lymphatic), nor were there any intraoperative adverse events related to the harmonic scalpel. In the postoperative period, there were no surgical site complications.

### Table 1. Patient Demographics

<table>
<thead>
<tr>
<th></th>
<th>Harmonic Scalpel (n = 17)</th>
<th>Traditional (n = 17)</th>
<th>Total, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at surgery, y, mean (SD)</td>
<td>60 (12.8)</td>
<td>59 (11.0)</td>
<td></td>
</tr>
<tr>
<td>Sex, No.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>13</td>
<td>13</td>
<td>26 (76)</td>
</tr>
<tr>
<td>Female</td>
<td>4</td>
<td>4</td>
<td>8 (24)</td>
</tr>
<tr>
<td>Body mass index, mean (SD)</td>
<td>26.6 (5.2)</td>
<td>28.6 (5.3)</td>
<td></td>
</tr>
<tr>
<td>Primary site, No.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral cavity</td>
<td>15</td>
<td>13</td>
<td>28 (82)</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>4</td>
<td>6 (18)</td>
</tr>
<tr>
<td>T stage, No.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>3</td>
<td>2</td>
<td>5 (15)</td>
</tr>
<tr>
<td>T2</td>
<td>12</td>
<td>10</td>
<td>22 (65)</td>
</tr>
<tr>
<td>T3</td>
<td>1</td>
<td>1</td>
<td>2 (6)</td>
</tr>
<tr>
<td>T4</td>
<td>1</td>
<td>4</td>
<td>5 (15)</td>
</tr>
<tr>
<td>N stage, No.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N0</td>
<td>5</td>
<td>8</td>
<td>13 (38)</td>
</tr>
<tr>
<td>N1</td>
<td>3</td>
<td>5</td>
<td>8 (24)</td>
</tr>
<tr>
<td>N2</td>
<td>8</td>
<td>4</td>
<td>12 (35)</td>
</tr>
<tr>
<td>N3</td>
<td>1</td>
<td>0</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Overall stage, No.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>0</td>
<td>2</td>
<td>2 (6)</td>
</tr>
<tr>
<td>II</td>
<td>5</td>
<td>5</td>
<td>10 (29)</td>
</tr>
<tr>
<td>III</td>
<td>3</td>
<td>2</td>
<td>5 (15)</td>
</tr>
<tr>
<td>IV</td>
<td>9</td>
<td>8</td>
<td>17 (50)</td>
</tr>
</tbody>
</table>

There were no significant differences between groups.
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(seroma, hematoma, wound infection). Other secondary outcomes are reported in Table 2. There were no differences between the harmonic scalpel and traditional groups.

Discussion

Blood transfusion and prolonged operating time are clearly associated with adverse outcomes in patients undergoing major head and neck surgical procedures. Strategies to reduce bleeding and operating time are therefore worth investigating, and in this randomized trial, we have shown that the harmonic scalpel significantly reduces blood loss in patients undergoing SND for HNSCC. There is a growing consensus in the surgical literature about the importance of minimizing intraoperative blood loss. A study by Urquhart et al.7 evaluated neck dissections over a 3-year period and demonstrated that total intraoperative blood loss is a strong predictor of the amount and duration of postoperative drainage. Furthermore, a study by Girod et al.8 demonstrated that perioperative blood transfusion was associated with a higher overall complication rate. Patients with HNSCC often require complex surgical resections and reconstruction, which inherently produce prolonged anesthetic and surgical times. Farwell et al.1 evaluated patients undergoing major head and neck surgery and identified 3 risk factors associated with postoperative complications: prolonged anesthesias times (longer than 8 hours), a history of hepatitis, and large-volume intraoperative fluid resuscitations. Since minimizing operative time and blood loss is important to reduce postoperative complications, new surgical techniques are being developed to enable surgeons to increase their speed and efficiency.

The harmonic scalpel is a surgical device that uses ultrasonic energy to simultaneously cut and coagulate tissue. Although developed initially for laparoscopic surgery, the harmonic scalpel has evolved over the years, and several studies have investigated the use of this device in a variety of head and neck procedures, including thyroidectomy,1 parotidectomy,10 submandibular gland excision,11 and neck dissections.4 These studies explored differences in operative time, blood loss, and postoperative pain when using the harmonic scalpel compared to various other surgical techniques. Although most studies conclude that the harmonic scalpel decreases both operative time and blood loss, the extent of improvement can vary depending on the specific procedure and patient population.

### Table 2. Clinical Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Harmonic Scalpel (n = 17)</th>
<th>Traditional (n = 17)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcomes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Operative time, min, mean (95% CI)</td>
<td>81 (73-89)</td>
<td>85 (70-100)</td>
<td>.5</td>
</tr>
<tr>
<td>Intraoperative blood loss, mL, mean (95% CI)</td>
<td>62 (31-92)</td>
<td>158 (52-265)</td>
<td>.02a</td>
</tr>
<tr>
<td><strong>Secondary outcomes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vascular complications</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Neurologic complications</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Surgical drain output, mean (95% CI)</td>
<td>143 (94-193)</td>
<td>129 (97-162)</td>
<td>.6</td>
</tr>
<tr>
<td>48 hours, mL</td>
<td>209 (121-297)</td>
<td>191 (132-250)</td>
<td>.7</td>
</tr>
<tr>
<td>1 week, mL</td>
<td>14 (11-17)</td>
<td>13 (9-17)</td>
<td>.7</td>
</tr>
</tbody>
</table>

Abbreviation: CI, confidence interval.

aWilcoxon.

Figure 2. Primary outcomes: (A) blood loss and (B) operating room (OR) time.
time and intraoperative blood loss, there are no randomized studies of level I to IV neck dissection in HNSCC that isolate the neck dissection from the primary organ ablation. These shortcomings make it difficult to evaluate the utility of the harmonic scalpel in neck dissection for patients with HNSCC.

Although the technological basis of the harmonic scalpel confers some advantages, potential disadvantages have been reported. In 2009, Mallur et al.12 performed 250 consecutive thyroidectomies with a harmonic scalpel and reported a considerable amount of heat generated from the handpiece, which caused occasional thermal injury to the surrounding skin, soft tissue, and surgical drapes. Furthermore, both Mallur et al.12 and Miccoli et al.13 have reported surgical instrument fractures due to the heat generated by the harmonic scalpel handpiece. Another factor limiting the use of the harmonic scalpel is the expense of the disposable handpieces in a time of growing concern over hospital waste and environmental preservation.14 Despite these concerns, a recent study by Lombardi et al.15 demonstrated a cost-effectiveness benefit for the harmonic scalpel during thyroidectomy, which was primarily attributed to a 30% reduction in operative time. However, there are no studies evaluating the cost-effectiveness of the harmonic scalpel in neck dissections, and no study has addressed the surgical waste dilemma.

Two randomized trials have evaluated the harmonic scalpel as an adjunct to neck dissection. Salami and colleagues studied the harmonic scalpel during radical neck dissection (RND) in conjunction with laryngopharyngectomy for advanced (T4/N2 or N3) laryngopharyngeal SCC. This study showed that the harmonic scalpel was an effective tool in reducing OR time and blood loss. However, blood loss was calculated from suction canister measurements, and it is unclear if intraoperative irrigation and sponge weights were considered in the blood loss calculations. In addition, the method of randomization is not specified by the authors. Therefore, the results of this study may not be comparable to ours. A 2009 study by Miccoli et al.15 published a randomized trial investigating the impact of the harmonic scalpel in treating patients with papillary thyroid cancer and neck metastases. The variables examined included thyroid volume, neck circumference, operative time, diameter of the tumor and lymph nodes, postoperative drainage, pain, and other complications. Their results demonstrated that operative time was significantly shorter in the harmonic scalpel group while reducing postoperative drainage (between 24 and 48 hours) and postoperative pain. There was no difference in the complications between the 2 groups (harmonic scalpel vs traditional technique). Since this study was restricted to patients with papillary thyroid cancer and also included a level V neck dissection, the results may not be directly comparable to ours.16 In addition to several methodological differences, none of the studies published to date used the Harmonic Focus handpiece, a device specially designed for head and neck surgical procedures. Therefore, despite these prior studies investigating the harmonic scalpel, the results of our study are important.

The results from this study demonstrate a significant reduction in blood loss in the harmonic scalpel group compared to the traditional technique group, 62 mL vs 158 mL, respectively ($P = .02$). We did not detect a difference in operative time between the harmonic scalpel and traditional technique, 81 minutes and 85 minutes, respectively ($P = .05$). When evaluating the impact of a new surgical instrument on operative time, it is important to consider the learning curve. Our study design, unlike others, included a “wash-in” period where both head and neck surgeons used the harmonic scalpel to perform a selective neck dissection 10 times before accruing patients. Furthermore, our final operative time calculation did not include the time spent during skin flap elevation. This is in contrast with the study by Kos and Engelke,4 where the operative time was recorded from the first incision to the final suture placement. We believe this is an important distinction since we rarely use the harmonic scalpel before the skin flaps are elevated. In our opinion, calculating the neck dissection operating time and excluding skin flap elevation and wound closure times more accurately evaluates the contribution of the harmonic scalpel to the procedure. Using this approach, we were able to isolate the harmonic scalpel’s impact on the neck dissection OR time and blood loss.

Although our study supports the use of the harmonic scalpel to reduce intraoperative blood loss, we, unlike other investigators, did not demonstrate a decrease in operative time. There are several potential reasons for this discrepancy. First, the present study was randomized and included only subjects undergoing level I to IV selective neck dissection. Our design isolated the neck dissection from other aspects of the procedure (ie, flap elevation), and this might have had an impact on overall operative time. Second, our study used the new Harmonic Focus handpiece. Other studies did not use this tool, and this could have had an influence on operative time. Finally, other studies did not isolate the neck dissection from the rest of the oncologic procedure.

Meticulous hemostasis is important, but there are clinical situations that require special attention to hemostasis such as a history of bleeding disorder, preoperative anemia, or in cases where a religious/moral aversion to receiving a blood transfusion exists. The harmonic scalpel may be particularly beneficial in these situations. However, at a cost of approximately $600 per handpiece, surgeons should carefully consider the clinical context before routinely using the harmonic scalpel for all head and neck surgical procedures.

Although our study design was robust, there are some limitations to this research. First, this was a single institutional study with 2 experienced head and neck surgeons performing the neck dissections. This potentially limits the generalizability of the findings. A multicenter study could reduce any surgical technique bias produced by evaluating surgeons from a single center. Second, although we showed a blood loss reduction of 100 mL in the harmonic scalpel arm of the study, the benefit of this reduction in clinical practice could be debated. Pertaining to the issue of blood loss, we did not take into account the possible effect that hemodilution may have had on the estimation of surgical blood loss. In the literature, there are mathematical models that are available to calculate surgical blood loss, which takes into account preoperative and postoperative hematocrit and the amount of hemodilution performed during the surgery. Failing to account for the confounding
effect of hemodilution, we may have underestimated the amount of surgical blood loss in both the harmonic scalpel and traditional arms of our study.11 No other studies of the harmonic scalpel in neck dissection have taken this factor into consideration, and we do not believe this failure invalidates our results. Finally, we did not perform a formal economic or environmental analysis of the harmonic scalpel’s impact on neck dissection. This analysis was not part of our study design but should definitely be part of further research on this topic. Despite these limitations, we believe our study contributes new knowledge that will enable surgeons to better select patients who will most benefit from a harmonic scalpel-assisted neck dissection.

Conclusions
Neck dissection is a common procedure during the management of patients with HNSCC. Our study shows that the harmonic scalpel is an effective tool for reducing intraoperative blood loss in patients undergoing SND for HNSCC, but it had no impact on operative time. Head and neck surgeons should consider using the harmonic scalpel in situations where minimizing blood loss is essential to a particular patient’s clinical outcome. More research needs to be done in evaluating the cost-benefit ratio of the harmonic scalpel in otolaryngology–head and neck surgical procedures. Such studies, using robust randomized methodologies, will determine the exact role of the harmonic scalpel in making our procedures faster and safer for our patients.

Author Contributions
Scott G. Walen, study conception and design, data acquisition, drafting and critical revisions, final approval; Luke R. Rudmik, study conception and design, data acquisition and interpretation, critical revisions, final approval; Elijah Dixon, study conception and design, data interpretation, critical revisions, final approval; T. Wayne Matthews, study conception and design, data acquisition and interpretation, critical revisions, final approval; Steven C. Nakoneshny, data acquisition, analysis and interpretation, drafting and critical revisions, final approval; Joseph C. Dort, study conception and design, data acquisition, analysis and interpretation, critical revisions, final approval.

Disclosures
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References