"One surgical advancement that may offer a solution to some of the complications associated with STS wide resection is the use of a hybrid plasma scalpel rather than traditional Bovie electrocautery."

Reduced Blood Loss With Use of Canady Hybrid Plasma Scalpel Compared With Bovie Electrocautery in the Resection of Soft-Tissue Sarcomas

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INTRODUCTION

As medicine continues to seek increasingly improved outcomes, many fields have developed novel and innovative treatments. The field of orthopedic oncology is no exception to this effort and as a result has seen notable changes in guidelines and research discoveries within the past 10 years, particularly in the treatment of soft-tissue tumors. Improvements in multidisciplinary care at large institutions over the years have paved the way for improved surgical treatment options that aim to conserve limb function through an improved understanding of the various histologic subtypes of musculoskeletal tumors.[1,2]

One of the more common malignancies orthopedic oncologists treat is soft-tissue sarcoma (STS). These tumors are a heterogeneous group that represent a small percentage of cancer diagnoses in the United States, with an incidence of 5 per 100 000 people per year.[2,3] STS comprises numerous different histopathologic subtypes with varying degrees of aggressiveness. These tumors can vary from low to high grade and are identified most commonly in the extremities and less commonly in axial distribution.[3] For many patients with STS, wide resection techniques offer curative treatment, often with adjuvant or neoadjuvant radiation treatment, depending on initial biopsy findings.[3] With current advances in the surgical resection of STS, improved radiation techniques, and the increasing use of limb salvage surgery, many patients have had improved functional outcomes.[4]

Despite these great advances, wide resection of STS still presents marked secondary causes of morbidity. The main complications associated with surgical treatment of STS are blood loss and wound complications, especially in cases with preoperative and/or postoperative radiotherapy.[5] Study results have shown that wound complications, including wound dehiscence, surgical site infections, hematomas, seromas, and necrosis, can occur in 16% to 56% of cases.[6,7] Furthermore, wide resection is associated with notably more blood loss than are marginal resections in the removal of malignant musculoskeletal tumors.[8]

One surgical advancement that may offer a solution to some of the complications associated with STS wide resection is the use of a hybrid plasma

Table 1. Patient Demographic Characteristics and Baseline Operative Information Compared Across Cohorts

Parameter	Bovie (n = 97)	Plasma (n = 40)	*P* Value
Female, No. (%)	53 (54.6)	18 (45)	.350[a]
Age at primary operation, y (SD)	54.86 (19.71)	55.95 (19.35)	.768[b]
Tumor location, No. (%)			
Lower extremity	68 (70.1)	29 (72.5)	1.000[a]
Upper extremity	24 (24.7)	10 (25.0)	
Axial	4 (4.1)	1 (2.5)	
Upper extremity/axial	1 (1.0)	0 (0)	
Procedure type, No. (%)			
Wide/limb salvage	81 (83.5)	32 (80.0)	.865[a]
Other	8 (8.3)	4 (10.0)	
Amputation	7 (7.2)	4 (10.0)	
Marginal resection	1 (1.0)	0 (0)	
Superficial lesion (vs deep), No. (%)	25 (25.8)	9 (22.5)	.829[a]
Lesion size, cm (SD)	14.64 (6.88)	15.92 (8.15)	.383[b]
Primary closure, No. (%)	79 (84.4)	32 (80.0)	.814[a]

[a]Results from Fisher exact test.
[b]Results from *t* test.

scalpel rather than traditional Bovie electrocautery. The Canady Hybrid Plasma Scalpel (CHPS) is a unique surgical tool that is capable of cutting and coagulating tissue simultaneously through its application of combined electrocautery and inert argon plasma.[9] Because of these features, the CHPS may offer hemostasis during surgery that is superior to that of traditional electrocautery and other perioperative methods, including bipolar sealer, antifibrinolytics, and hemostatic agents. For example, in patients who underwent direct anterior total hip arthroplasty, those whose operation included the CHPS demonstrated significantly smaller decreases in postoperative blood hemoglobin levels and measured blood loss than those in which the surgeon used bipolar sealer.[9] Other applications of the CHPS demonstrated thermal properties of sterilization and coagulation that were the same as or superior to that of Bovie electrocautery but without the damage to normal healthy tissue.[10]

In addition, surgeons have expressed interest in using the CHPS for its therapeutic anticancer properties in the resection of solid tumor masses. The CHPS can apply inert argon gas as cold atmospheric plasma (CAP), now considered a major therapeutic option for the treatment of solid tumor masses. Specifically, CAP selectively eradicates various types of cancer cells, including lung, bladder, and hepatocellular carcinomas, as well as brain and other head and neck cancers, both in vitro and in vivo, without damaging nearby healthy cells.[11,12] CAP may be able to eradicate cancer cells selectively by preferentially targeting rapidly dividing cells by deregulating genes responsible for reactive oxygen species (ROS) metabolism and oxidative stress response.[13] Although some study results have demonstrated that the CHPS offers a therapeutic advantage over traditional electrocautery in the resection of various solid tumors, whether these advantages apply to the outcomes of patients with STS is currently unknown.

The primary purpose of this retrospective study was to compare the outcomes of patients with STS who underwent resection with either Bovie electrocautery or the CHPS. We hypothesized that patients who undergo STS wide resection with the CHPS would have less blood loss, shorter operative time, and lower rates of wound complications and local recurrence than would patients who underwent STS wide resection with Bovie electrocautery. Our secondary outcomes were to review the disease-related outcomes in both groups, including local recurrence, metastases, and overall survival.

METHODS

The Rush Institutional Review Board approved this study before commencement. We obtained data obtained retrospectively through the medical charts of 137 patients who underwent resection of an STS during 2010 through 2018. The patient population consisted of 2 cohorts—97 patients who underwent resection by means of Bovie electrocautery during the period from 2010 through 2015 and 40 patients who underwent resection by means of the CHPS after 2015. We examined multiple data points for every patient at the time of surgery, including baseline demographic characteristics, procedure type, duration of operation, type of scalpel used, intraoperative blood loss, amounts and types of blood products transfused, size of lesion, depth of lesion, type of wound closure, and histopathologic findings. Secondary outcome measures included development of local recurrence, development of metastasis, need for adjuvant therapy after primary surgery, duration of operation, hematoma formation, seroma formation, surgical site infection, fatality, negative margins, blood products transfused, adjuvant therapy after primary surgery, and development of wound complications. The primary outcome measure was intraoperative blood loss.

For the univariate analysis, we used the Fisher exact test for categorical variables and a *t* test for continuous variables. We used regression analysis to evaluate the primary outcome measure, intraoperative blood loss. We had considered logistic and linear regression analyses for the secondary outcome measures, but they were not fruitful, so we used univariate analysis. We performed all analyses using Stata/IC 14.2 (StataCorp LLC; College Station, Texas) and set significance at α of .05.

RESULTS

We compared patient demographic characteristics and baseline operative information across the CHPS and Bovie cohorts; the 2 cohorts were equivalent on all noted baseline variables, as shown in Table 1. Therefore, we consider the 2 cohorts to be comparable.

We compared the secondary outcome measures by using univariate analysis; we found that the 2 cohorts were not statistically different according to any of these measures, as shown in Table 2. Specifically, the length of surgery was not statistically different, with the average Bovie cohort operation lasting almost 91 minutes and the average plasma cohort operation lasting more than 95 minutes (P = .74). Also, 9 (9.4%) of 96 patients in the Bovie cohort and 1 (2.5%) of 40 patients in the plasma cohort (P = .28) had surgical site infection; 8 (8.3%) patients in the Bovie cohort and 1 (2.5%) in the plasma cohort (P = .28) had seroma formation; 11 (12.1%) patients in the Bovie cohort and 5 (12.5%) in the plasma group developed a local recurrence (P = 1.00); and 30 (34.1%) patients in the Bovie cohort and 9 (22.5%) in the plasma group developed metastasis (P = .22).

For the primary outcome measure, intraoperative blood loss, we used a linear regression, as shown in Table 3; we used the length of the operation and the size of the lesion as confounding factors. We also incorporated a second-

Table 2. Secondary Outcome Measures Compared Across Cohorts

Outcome Measure	Bovie (n = 97)	Plasma (n = 40)	*P* Value
Wound complications, No. (%)	22 (22.9)	7 (17.5)	.646[a]
Seroma formation, No. (%)	8 (8.3)	1 (2.5)	.282[a]
Hematoma formation, No. (%)	4 (4.2)	3 (7.5)	.419[a]
Surgical site infection, No. (%)	9 (9.4)	1 (2.5)	.280[a]
Metastasis, No. (%)	30 (34.1)	9 (22.5)	.218[a]
Local recurrence, No. (%)	11 (12.1)	5 (12.5)	1.000[a]
Fatality, No. (%)	9 (9.8)	5 (12.5)	0.759[a]
Negative margins, No. (%)	92 (94.8)	38 (95.0)	1.000[a]
Blood products received, No. (%)	22 (22.7)	8 (20.0)	.823[a]
Adjuvant therapy after primary surgery, No. (%)	60 (61.9)	22 (55.0)	.151[a]
Duration of operation, min (SD)	90.98 (68.85)	95.18 (62.41)	.740[b]

[a]Results from Fisher exact test.
[b]Results from *t* test.

Table 3. Regression Analysis of Primary Outcome (Intraoperative Blood Loss)[a]

Variable in Regression	Coefficient	*P* Value	95% CI
Duration of operation	1.05	< .001	0.58-1.53
Duration of operation squared (second-order term)	−0.17	.006	−0.20- −0.03
Use of CHPS	−0.75	< .001	−1.12- −0.38
Size of lesion	0.08	< .001	0.05-0.11
Constant	2.69	< .001	2.13-3.24

[a]This regression was log-transformed so the dependent response variable was the natural logarithm of blood less (lnblood loss).
Abbreviations: CHPS, Canady Hybrid Plasma Scalpel; CI, confidence interval.

order factor for length of surgery because of the nonlinear relationship between operation duration and blood loss. The assumption of normality of residuals was not valid; therefore, we used a logarithmic transformation, and the resulting logarithmic-linear model is valid. From this model, we can conclude that the use of the CHPS reduced blood loss by 52.9% (95% CI: 31.8%-67.4%; $P < .001$) (Figure). Assuming the average operation duration and lesion size, this difference equates to an approximately 95-mL reduction in operations with the CHPS in our data set.

DISCUSSION

With an incidence of 5 per 100 000 people per year, STS account for only 1% of all cancer diagnoses yearly.[3,14] Overall, STS comprises more than 50 different histologic subtypes and can vary from low to high grade.[1] High-grade lesions can be associated with a mortality rate of 40% to 60%.[15] Most patients have tumors diagnosed in the extremities and less frequently in the trunk, retroperitoneum, and head and neck areas, and most have a clinical presentation of a painless, gradually enlarging mass.[3] With better understanding of the various histologic subtypes and their natural history, the recognized consensus for treatment of these musculoskeletal tumors is first to biopsy the tumor and, if histopathologic diagnosis does not demonstrate the tumor to be high grade, the recommendation is to proceed to with wide surgical resection.[3] Over the years, the trend toward limb salvage surgery in the treatment of STS has led to increased functional outcomes in many patients. Although many patients have been successfully treated, some patients who undergo wide surgical resection still experience significant morbidity in the form of blood loss, prolonged hospital stays, and wound complications.

Many medical disciplines, including orthopedics, have turned to newer methods to improve intraoperative hemostasis; in some instances, the CHPS was superior for the control of blood loss[9]. When compared with bipolar sealer and traditional Bovie electrocautery, the CHPS significantly reduced blood loss intraoperatively when measured through both hemoglobin and hematocrit levels and actual counted blood loss. Furthermore, the authors found that the CHPS significantly reduced the length of operations when compared with the other hemostatic methods measured, which may mirror any intraoperative complications, including hemostasis control.

Patients in this study who underwent STS wide resection with the CHPS lost significantly less blood than did those who underwent resection with Bovie electrocautery, as measured by estimated intraoperative blood loss. Increased perioperative blood loss in orthopedic and oncologic surgery is well known to increase mortality and morbidity.[16] Perioperative blood transfusion in cancer resection also has been associated with worse outcomes and increased risk of disease recurrence because of the immunosuppressive nature of allogeneic products.[17,18] Therefore, the ability of the CHPS to significantly reduce perioperative blood loss in patients undergoing STS wide resection should translate to improvements in some secondary outcomes, including length of stay and mortality from major noncardiac operations; however, we did not confirm this finding in our study, possibly because of the limited sample size.

Although our study's results did not show any statistically significant difference in overall complication rates, we saw a decreased percentage of wound complications, seromas, and surgical site infections in the CHPS group.

The CHPS can offer many other benefits besides improved hemostasis in patients undergoing surgery for musculoskeletal tumors. The application of inert argon gas from the CHPS (ie, CAP) can induce preferential malignant necrotic cell death, leading to the recently recognized field of plasma oncology.[19,20] Results from 1 study showed that CAP can both target cancer cells and reduce tumor size in various cancer cell

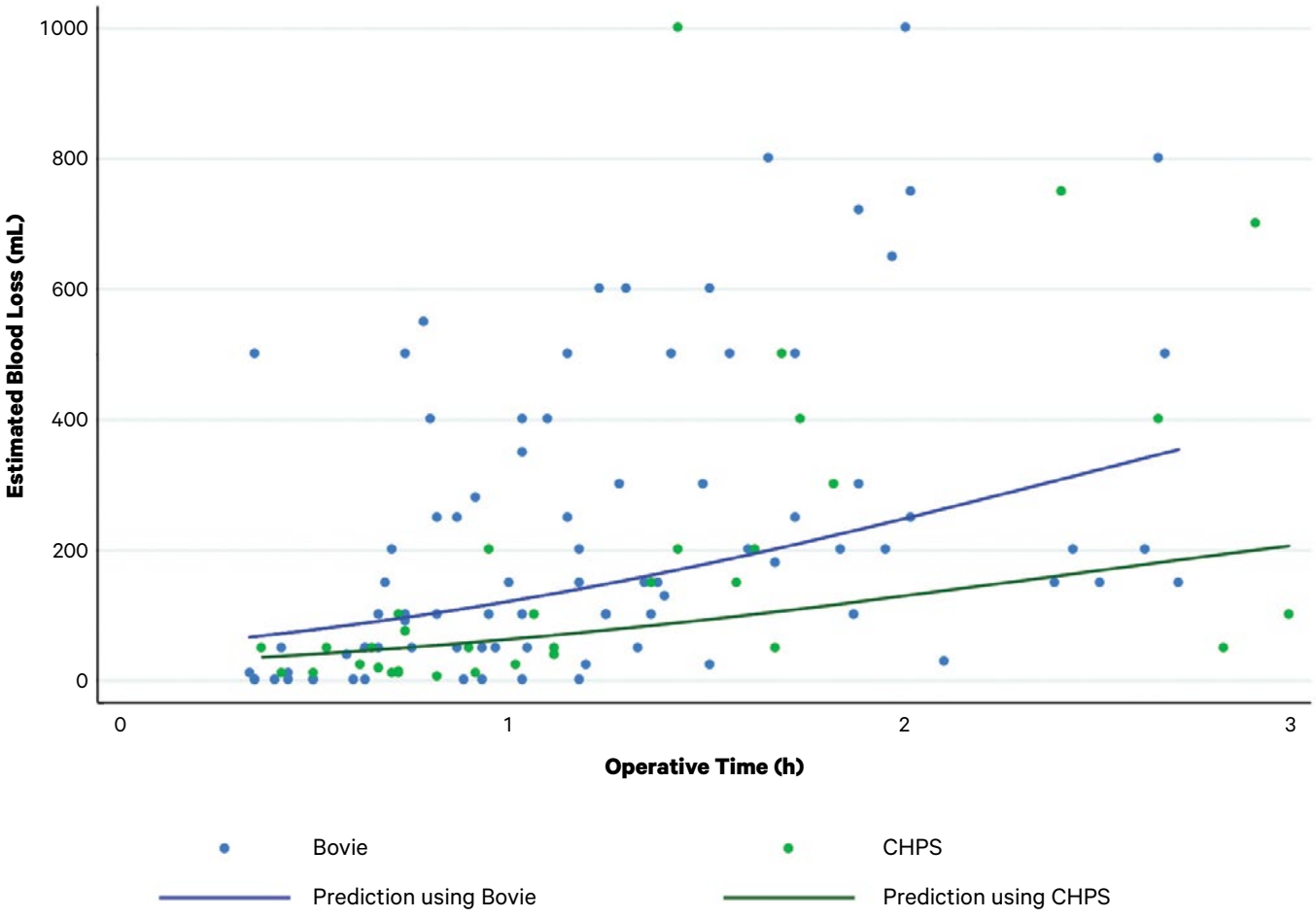

Figure. Estimated Intraoperative Blood Loss Comparison Between Bovie Electrocautery and Canady Hybrid Plasma Scalpel (CHPS)

lines, including lung, bladder, skin, and brain and other head and neck cancers, suggesting that application of CAP offers a major paradigm shift in the surgical treatment of cancer.[12] Volotskova et al[13] hypothesized that CAP is able to eradicate cancer cells selectively by preferentially targeting rapidly dividing cells and deregulating key genes in malignant cells that are responsible for ROS metabolism and the oxidative stress response. Tumor cells at baseline are under increased oxidative stress because of the increased gene activation and cell division; investigators in 2 studies[19,21] have hypothesized that this characteristic makes them more vulnerable to the additional exposure to oxidants, in this case CAP-induced increase of ROS. Although our study's results did not show any statistically significant difference between the rates of local recurrence, metastases, or survival in the comparison of the Bovie electrocautery cohort and the CHPS cohort, the CHPS group had a decreased percentage of metastases.

CONCLUSION

The purpose of this study was to investigate whether the CHPS improves outcomes in patients undergoing resection of STS. Overall, we showed that the CHPS was associated significantly with reduced blood loss intraoperatively. Both groups had similar rates of transfused blood products and postoperative complications, including wound infections, seromas, and metastases. Future studies with increased sample sizes are needed to determine whether there are beneficial effects of the CHPS in the treatment of STS. Future studies of CAP treatment of sarcoma at the molecular level also may be beneficial to understanding the potential benefits of treatment with the CHPS. ✻

References and financial disclosures are available online at www.rush.edu/orthopedicsjournal.