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Naoya Ikeda *

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Total Sealing Technique in Axillary Lymph Node Dissection for Breast Cancer: A Comprehensive Review of Clinical Outcomes and Health Economic Value

Naoya Ikeda [1,2]

[1] Department of Surgery, KIWA Hospital, Wakayama 648-0085, Japan; n-ikeda@naramed-u.ac.jp; Tel.: +81-736-33-5000

[2] Department of Forensic Medicine, Wakayama Medical University, Wakayama 641-8509, Japan

Simple Summary

Axillary lymph node dissection (ALND) remains necessary for selected patients with breast cancer but is frequently associated with postoperative complications, including seroma, prolonged hospital stay, and breast cancer–related lymphedema (BCRL), which can impair long-term quality of life and increase healthcare costs. This review focuses on the Total Sealing Technique (TST), a technique-centered approach to ALND that emphasizes systematic sealing of lymphatic and vascular structures rather than simple device substitution. Available evidence indicates that TST reduces postoperative drainage, shortens hospital stay, decreases seroma, and markedly lowers the incidence of BCRL. By addressing both early postoperative complications and long-term lymphatic morbidity at the time of initial surgery, TST offers a pragmatic strategy to improve patient recovery while reducing healthcare resource utilization and downstream costs. As contemporary breast cancer care increasingly prioritizes survivorship, quality of life, and value-based outcomes, technique-driven innovations may contribute to safer and more sustainable axillary surgery.

Abstract

Background/Objectives: Axillary lymph node dissection (ALND) remains an essential component of breast cancer surgery for selected patients, particularly those with clinically involved nodes or residual disease after neoadjuvant therapy. However, ALND is consistently associated with postoperative lymphatic morbidity, including seroma formation, prolonged drainage, and breast cancer–related lymphedema (BCRL), which adversely affect quality of life and increase healthcare utilization. This review aims to evaluate contemporary ALND strategies with a particular focus on the Total Sealing Technique (TST), a technique-centered approach that emphasizes comprehensive lymphatic sealing rather than device substitution. **Methods:** A narrative review of the literature was conducted to synthesize available experimental, histopathological, and clinical evidence related to TST. Studies evaluating biological mechanisms, perioperative outcomes, long-term lymphatic complications, and health economic implications of TST were reviewed and contextualized alongside data from conventional electrocautery-based techniques and energy-device substitution strategies. **Results:** Across published studies, TST is consistently associated with reductions in postoperative drainage volume, duration of drain placement, incidence of seroma formation, and length of hospital stay. Importantly, long-term follow-up data demonstrate a marked reduction in the incidence of BCRL compared with conventional ALND techniques. These benefits are achieved without increases in operative time, perioperative complications, or compromise of oncological safety. From a health economic perspective, reductions in inpatient hospitalization, outpatient seroma management, and long-term lymphedema-related care translate into meaningful per-patient cost savings. **Conclusions:** The available evidence supports TST as a reproducible and scalable surgical strategy that effectively reduces both short-term postoperative morbidity and long-term lymphatic complications following

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ALND. By addressing lymphatic injury at the time of initial surgery, TST aligns with contemporary priorities in breast cancer care, including survivorship, quality of life, and value-based healthcare delivery.

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1. Introduction

Breast cancer is the most commonly diagnosed cancer in women worldwide and remains a major contributor to cancer-related morbidity and mortality, accounting for an estimated 2.3 million new cases and 670,000 deaths globally in 2022, with incidence rising in many countries and mortality disparities across regions[1]. Surgical treatment remains fundamental to curative intent, providing local disease control while enabling accurate pathological staging to guide adjuvant systemic and radiation therapies. Despite its oncological value, axillary lymph node dissection (ALND) is associated with substantial short- and long-term morbidity [2,3]. Among postoperative complications, lymphorrhea and seroma formation are the most common early adverse events, frequently resulting in prolonged drainage, delayed discharge, repeated outpatient visits, and impaired patient satisfaction. More importantly, breast cancer–related lymphedema (BCRL) represents a chronic and often irreversible condition that may persist for decades after surgery, adversely affecting physical function, psychological well-being, social participation, and overall quality of life, while imposing a significant and lifelong economic burden on both patients and healthcare systems [2,4]. Large prospective cohort studies have demonstrated a clear association between the extent of axillary intervention and the cumulative incidence of BCRL. Naoum et al. reported that five-year BCRL incidence increases from approximately 8–11% after sentinel lymph node biopsy–based strategies to more than 25–30% following ALND combined with regional nodal irradiation. These findings underscore that, even in the modern era of de-escalated axillary surgery, a substantial proportion of breast cancer survivors remain at risk of BCRL due to the continued necessity of ALND in selected patient populations [3]. From a healthcare economics perspective, postoperative morbidity following ALND has consequences that extend far beyond the operating room. Prolonged hospitalization increases immediate inpatient costs, while seroma-related complications generate repeated outpatient visits, imaging studies, and procedural interventions. In the long term, BCRL requires ongoing management with compression therapy, physical therapy, outpatient surveillance, and, in selected cases, surgical intervention. Multiple cost analyses have demonstrated that patients who develop BCRL incur significantly higher cumulative healthcare expenditures than those who do not, highlighting the economic importance of effective preventive strategies [2,4–6]. Conventional ALND is most commonly performed using monopolar electrocautery, a technique widely adopted since the 1970s because of its effectiveness in achieving hemostasis and facilitating tissue dissection. However, electrocautery is associated with incomplete sealing of lymphatic channels and collateral thermal injury to surrounding tissues. Experimental and clinical studies suggest that thermally injured lymphatic vessels may reopen postoperatively, leading to persistent lymphatic leakage, seroma formation, and chronic inflammatory changes that predispose patients to subsequent BCRL [5,7]. From a clinical standpoint, bipolar vessel-sealing systems such as LigaSure™ provide a reproducible method for controlling lymphatic and vascular structures during axillary dissection. By enabling consistent sealing across tissue bundles, these devices have been associated with reductions in postoperative drainage volume, earlier drain removal, and shorter hospital stay—outcomes that directly influence perioperative recovery and healthcare resource utilization [5,8,9]. Nevertheless, most prior studies have focused on device-to-device comparisons rather than on the underlying surgical concept. Reported outcomes have varied widely, likely reflecting heterogeneity in surgical technique, extent of sealing, and surgeon-dependent factors. Importantly, few studies have examined whether refinement of axillary dissection

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technique itself can meaningfully reduce the incidence of BCRL or translate into sustained health economic benefit [5,6]. Against this background, we introduced the Total Sealing Technique (TST), a standardized surgical approach to ALND that applies a bipolar vessel-sealing system to systematically seal all dissected tissues prior to transection. Unlike conventional approaches that selectively seal visible vessels, TST aims to comprehensively close microlymphatic channels embedded within axillary adipose tissue. In previous clinical studies, TST was associated with marked reductions in lymphorrhea, seroma formation, postoperative length of hospital stay, and—most notably—the incidence of BCRL [5,10]. The present review synthesizes current evidence on ALND techniques with a particular focus on TST using LigaSure™ Exact. By integrating data from clinical studies and meta-analyses of energy-based devices and contextualizing these findings within a health economic framework, we aim to demonstrate how optimization of surgical technique can simultaneously improve patient outcomes and reduce healthcare costs. This review is intended to provide clinicians, researchers, and policymakers with a comprehensive perspective on the potential role of TST in redefining the quality and value of modern axillary surgery.

2. Pathophysiology of Postoperative Morbidity After ALND

Axillary lymph node dissection disrupts a complex network of lymphatic channels, venous tributaries, nerves, and adipose tissue within the axilla. The immediate and long-term morbidities observed after ALND are the cumulative result of mechanical disruption, thermal injury, inflammatory response, and subsequent tissue remodeling [2,4,7]. Understanding this pathophysiology is essential for appreciating why refinements in surgical technique—rather than device substitution alone—may fundamentally alter postoperative outcomes.

2.1. Lymphorrhea and Seroma Formation

Lymphorrhea represents persistent leakage of lymphatic fluid from disrupted lymphatic channels following ALND. Unlike blood vessels, lymphatic vessels possess thin walls with minimal smooth muscle and lack intrinsic clotting mechanisms, making them particularly susceptible to postoperative leakage [5,11]. Accordingly, effective and durable intraoperative sealing of lymphatic channels is a critical determinant of postoperative lymphatic morbidity. Conventional monopolar electrocautery achieves hemostasis primarily through thermal coagulation; however, this same mechanism often results in incomplete and unstable closure of lymphatic channels. Experimental burst pressure testing has demonstrated inferior sealing strength with monopolar instruments compared with advanced energy-based devices. In porcine thoracic duct models, monopolar scissors exhibited immediate seal failure rates as high as 33%, with significantly lower burst pressures than bipolar or ultrasonic systems [12]. These experimental findings suggest that monopolar devices may be inherently less reliable for lymphatic sealing and therefore contribute to persistent lymphatic leakage, lymphorrhea, and subsequent seroma formation after ALND. Seroma formation represents the clinical manifestation of ongoing lymphorrhea combined with inflammatory exudation. Identified risk factors include the extent of axillary dissection, surgical technique, electrocautery use, and patient-related factors such as obesity. Moderate-quality evidence indicates higher seroma rates in patients with greater early postoperative drainage volumes and more extensive surgical dissection [13,14]. The clinical impact of seroma is substantial, as repeated percutaneous aspirations increase the risk of surgical site infection and may delay initiation of adjuvant systemic therapy or radiotherapy [5].

2.2. Inflammatory Response and Tissue Injury

The incidence of seroma has also been shown to vary according to surgeon-related factors, underscoring the role of operative technique [15]. A key contributor is thermal injury associated with surgical energy devices. Monopolar electrocautery generates lateral thermal spread beyond the immediate dissection plane, resulting in collateral tissue injury [7,16]. Thermal injury induces

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adipocyte necrosis, microvascular thrombosis, and release of pro-inflammatory cytokines, thereby amplifying capillary permeability and interstitial fluid exudation [17,18]. Persistent inflammation and subsequent fibrosis within the axilla may further compromise collateral lymphatic pathways and reduce compensatory drainage capacity, exacerbating lymphatic dysfunction [4].

2.3. Breast Cancer–Related Lymphedema (BCRL)

Breast cancer–related lymphedema is a progressive and often irreversible condition characterized by chronic limb swelling, fibrosis, and adipose deposition. Its pathogenesis is multifactorial, involving reduced lymphatic transport capacity, increased lymphatic load, and impaired lymphangiogenesis [4]. ALND remains one of the strongest independent risk factors for BCRL, particularly when combined with regional nodal irradiation [3]. Importantly, accumulating evidence suggests that the incidence of BCRL is strongly influenced by surgical technique and surgeon-dependent factors. From a biological perspective, the extent and quality of lymphatic injury incurred during ALND determine the residual functional lymphatic reserve within the axilla. Use of monopolar electrocautery may represent a major modifiable risk factor for BCRL, as its lateral thermal spread can damage perilymphatic tissues beyond the intended dissection plane. Heat-induced injury promotes chronic inflammation, fibrosis, and obliteration of microlymphatic channels, thereby impairing compensatory lymphatic drainage and predisposing patients to progressive lymphatic failure. Conversely, surgical strategies that minimize collateral thermal injury while achieving comprehensive lymphatic sealing may better preserve microlymphatic continuity and lymphatic reserve. In this context, technique-centered approaches emphasizing precise dissection and controlled energy delivery offer a biologically plausible means of reducing long-term BCRL risk [10,19].

3. Conventional Electrocautery Versus Energy-Based Devices

3.1. Conventional Electrocautery in Axillary Surgery

Monopolar electrocautery has long been used as a standard technique for tissue dissection and hemostasis in modified radical mastectomy because of its simplicity, availability, and effectiveness in reducing intraoperative blood loss [20,21]. However, the biological effects of electrocautery extend beyond vessel coagulation. Temperatures exceeding 200°C can induce tissue carbonization, fat necrosis, and collateral thermal injury to adjacent lymphatic and neural structures [7]. Experimental studies have demonstrated that lymphatic channels closed by thermal coagulation may reopen during the postoperative period, leading to persistent lymphorrhea. Clinically, this manifests as increased drain output, prolonged drain duration, and a higher incidence of seroma formation following ALND [10,11].

3.2. Limitations of Conventional Techniques

The limitations of electrocautery-based ALND become evident when postoperative outcomes are examined in detail. Observational studies have reported seroma rates ranging from 15% to more than 60% following conventional ALND [13,18]. Such wide variation reflects not only patient-related factors but also surgeon-dependent differences in technique. These include the extent of cautery use, traction applied to lymphatic tissue, and adequacy of vessel ligation [15]. From a systems perspective, the absence of a standardized approach to lymphatic control results in inconsistent outcomes across institutions and surgeons. This variability complicates quality improvement initiatives, benchmarking efforts, and the implementation of value-based surgical care [22].

3.3. Bipolar Vessel-Sealing Systems (LigaSure™ Exact)

From a clinical standpoint, bipolar vessel-sealing systems such as LigaSure™ provide a reproducible method for controlling lymphatic and vascular structures during axillary dissection. By

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enabling consistent sealing across tissue bundles, these devices have been associated with reductions in postoperative drainage volume, earlier drain removal, and shorter hospital stay—outcomes that directly influence perioperative recovery and healthcare resource utilization [5,8,9]. Clinical trials and meta-analyses have consistently demonstrated that LigaSure™ reduces postoperative drain volume and duration compared with conventional techniques. The meta-analysis by Imran et al., which synthesized data from randomized and observational studies, confirmed significant reductions in drainage volume, drain duration, and length of hospital stay without increases in operative time or complication rates [8,9,23]. Nevertheless, most studies evaluating LigaSure™ have treated the device primarily as a substitute for electrocautery rather than as part of a comprehensive surgical strategy. Surgeons often employ hybrid approaches, combining bipolar sealing for selected vessels with electrocautery for general dissection, which may dilute the potential benefits of complete lymphatic sealing [5,10].

3.4. Ultrasonic Devices (Harmonic®)

Ultrasonic devices represent an alternative energy-based approach. Harmonic® technology uses high-frequency mechanical vibration to cut and coagulate tissue at temperatures lower than those generated by electrocautery, thereby reducing lateral thermal spread [24,25]. Multiple randomized trials and meta-analyses have evaluated Harmonic® devices in breast cancer surgery. Meta-analyses by Huang et al. and Cheng et al. demonstrated significant reductions in postoperative drainage volume, seroma formation, intraoperative blood loss, and wound complications compared with electrocautery, with modest reductions in length of hospital stay in some studies [26,27]. However, similar to LigaSure™, Harmonic® devices have primarily been assessed as tools rather than as components of a standardized operative concept. Reported outcomes vary widely, reflecting heterogeneity in surgical technique, workflow, and outcome definitions [26]. Moreover, long-term endpoints such as breast cancer–related lymphedema are rarely included in Harmonic® studies, limiting conclusions regarding sustained benefit [4].

3.5. Lessons from Energy-Based Device Studies

Collectively, studies of LigaSure™ and Harmonic® demonstrate that improved control of lymphatic and vascular structures can reduce early postoperative morbidity after ALND [5,23,28]. However, these studies also underscore a critical limitation: technological innovation alone does not guarantee optimal outcomes. Without a standardized operative concept guiding the extent and consistency of lymphatic sealing, the full potential of energy-based devices may not be realized. These observations provided the conceptual foundation for the development of the Total Sealing Technique, which reframes energy-based devices as integral components of a comprehensive, reproducible surgical strategy rather than as interchangeable tools [5,10].

4. Total Sealing Technique (TST): Concept, Technique, and Rationale

4.1. Conceptual Basis of the Total Sealing Technique

The Total Sealing Technique (TST) was developed to address a fundamental limitation of conventional axillary lymph node dissection, namely the incomplete and inconsistent sealing of lymphatic channels. Traditional approaches emphasize hemostasis, whereas lymphatic control has remained comparatively under-addressed despite its central role in postoperative morbidity. In contrast, TST is predicated on the principle that lymphatic sealing must be the primary objective of ALND, given that lymphatic injury is the principal driver of postoperative morbidity [5]. Rather than selectively sealing only visible vessels, TST applies a bipolar vessel-sealing system (LigaSure™ Exact) systematically to all tissues designated for dissection prior to transection. This comprehensive strategy ensures closure of both macroscopic lymphatic trunks and microscopic lymphatic channels

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embedded within axillary adipose tissue, thereby interrupting the cascade from lymphatic leakage to chronic inflammation and long-term lymphatic failure [10].

4.2. Surgical Technique and Standardization

TST is performed using a bipolar vessel-sealing device, most commonly the LigaSure™ Exact Dissector. Following identification of key anatomical landmarks, dissection proceeds along natural tissue planes, with each tissue bundle grasped, sealed, and divided in a consistent sequence. Monopolar electrocautery and suture ligation are deliberately avoided in order to maintain uniformity of lymphatic control throughout the axilla [5]. A defining feature of TST is its reproducibility. The seal–divide–advance sequence is repeated systematically, reducing surgeon-dependent variability and facilitating standardization across operators and institutions. Importantly, this approach does not require additional operative steps or specialized microsurgical training beyond familiarity with bipolar sealing devices, supporting its scalability and broad dissemination [5].

4.3. LigaSure™ Exact Dissector (LGSED)

The LigaSure™ Exact Dissector (LGSED) plays a critical role in the performance of TST.

Bipolar coagulation devices of the LigaSure™ family permanently seal blood vessels, lymphatic vessels, and tissue bundles through denaturation of collagen and elastin within the vessel wall, thereby enabling ligation-free surgery. Introduced in 2018, the LGSED represents the latest generation of these devices and incorporates several refinements optimized for meticulous axillary dissection. Notably, the LGSED features a narrow jaw width of 2 mm and an extended sealing length of 20.6 mm, allowing precise dissection and controlled separation of lymph nodes from adjacent vascular and neural structures. Despite its slim and elongated jaw design, the LGSED reliably seals vessels up to 7 mm in diameter, including surrounding connective tissue. Thermographic analyses reported by Campbell et al. demonstrated that lateral thermal injury was limited to approximately 1.8 mm from the device, with jaw surface temperatures remaining within a safe surgical range of approximately 35 °C [17]. This minimal thermal spread contrasts with that of conventional monopolar electrocautery and is particularly relevant in the axilla, where excessive heat diffusion may damage microlymphatic channels and predispose patients to postoperative lymphatic complications. Collectively, these characteristics allow the LGSED to function as both an effective sealing instrument and a precise dissecting tool, which is integral to the successful execution of TST.

4.4. Histopathological and Biological Rationale

Histopathological examination of treated specimens has provided direct evidence of successful lymphatic wall fusion and durable luminal obliteration mediated by the LGSED [5]. Unlike conventional thermal coagulation, which often produces fragile eschars prone to secondary breakdown, bipolar vessel sealing induces the formation of a stable protein matrix that resists postoperative reopening. Microscopic evaluation of lymphatic vessels sealed with the LGSED demonstrated complete fusion of the vessel walls without evidence of necrosis, secondary bleeding, or thrombus formation. Histological analyses revealed an adherent fibro-inflammatory pseudomembrane layer covering the sealed site, consistent with an organized healing response rather than indiscriminate thermal injury. Elastica van Gieson staining further demonstrated preservation of the internal elastic lamina and formation of dense collagen bundles bridging the obliterated lumen, indicating structural reinforcement of the sealed lymphatic channel. These findings provide a compelling biological rationale for the sustained reductions in lymphorrhea and seroma formation observed clinically, and support the long-term integrity of lymphatic occlusion achieved with TST.

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4.5. Clinical Outcomes Associated with TST

Across published clinical studies, TST has consistently demonstrated superior postoperative outcomes compared with conventional electrocautery-based ALND.

Reported benefits include significant reductions in total drainage volume, shorter duration of drain placement, lower seroma incidence, and meaningful decreases in length of hospital stay. These improvements reflect enhanced control of lymphatic leakage and more rapid postoperative recovery. Importantly, these favorable outcomes have been achieved without increases in operative time, intraoperative blood loss, or perioperative complication rates, indicating that improved lymphatic control does not compromise surgical efficiency or safety [5].

4.6. Impact of TST on Breast Cancer–Related Lymphedema

The most clinically meaningful advantage of TST is its association with a markedly reduced incidence of breast cancer–related lymphedema (BCRL). Long-term follow-up studies have demonstrated a reduction in cumulative BCRL incidence from 22.2% with conventional electrocautery-based ALND to 2.9% with TST, representing a substantial absolute and relative risk reduction [10]. This degree of risk mitigation exceeds that reported for most adjunctive preventive strategies and underscores the critical importance of the initial surgical technique in determining long-term lymphatic outcomes [2,4]. By minimizing lymphatic injury and postoperative inflammation at the time of axillary dissection, TST appears to preserve residual lymphatic reserve and reduce the likelihood of irreversible lymphatic failure. Collectively, these data reinforce the concept that primary prevention of BCRL is most effectively achieved through optimization of the axillary dissection technique itself, rather than reliance on secondary or tertiary interventions after lymphatic damage has occurred.

5. Comparative Analysis of Clinical Outcomes: TST Versus Harmonic and Conventional Techniques

5.1. Length of Hospital Stay

Meta-analyses evaluating Harmonic® technology in breast cancer surgery have demonstrated statistically significant but modest reductions in postoperative length of hospital stay, typically on the order of approximately 1.38 days, corresponding to an estimated 20–25% decrease compared with conventional electrocautery-based techniques [28]. These improvements have generally been attributed to reductions in postoperative drainage volume and earlier drain removal, reflecting the ability of ultrasonic energy devices to limit tissue trauma relative to monopolar electrocautery. Similar trends have been observed with bipolar vessel-sealing systems. In the most comprehensive systematic review and meta-analysis to date, Imran et al. analyzed outcomes from randomized and observational studies comparing LigaSure™ with conventional techniques in axillary lymph node dissection. The pooled analysis demonstrated that the LigaSure™ group experienced a reduction in length of hospital stay of 1.51 days (20.6%) compared with the traditional approach [23]. In contrast, the Total Sealing Technique (TST) is associated with a substantially greater reduction in postoperative hospitalization, with a mean decrease of 3.7 days, exceeding the magnitude of hospital stay reduction reported in both Harmonic®-based and LigaSure™-based meta-analyses by more than twofold [5]. This pronounced difference suggests that reductions in hospital stay are not determined solely by the choice of energy device, but rather by the comprehensiveness and consistency of lymphatic control achieved during axillary dissection. Whereas Harmonic® and LigaSure™ technologies are frequently employed as device substitutions within otherwise conventional or hybrid dissection workflows, TST represents a technique-centered strategy that emphasizes systematic sealing of all lymphatic and vascular structures designated for division during ALND. This approach results in more effective suppression of lymphatic leakage, earlier drain removal, and faster functional recovery, thereby enabling earlier readiness for discharge. Collectively, these findings indicate that optimization of

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surgical technique, rather than device substitution alone, is a key determinant of clinically meaningful reductions in length of hospital stay.

5.2. Seroma Formation and Management

While Harmonic® devices have been reported to reduce the incidence of postoperative seroma compared with conventional electrocautery, outcomes across published studies remain heterogeneous. Meta-analyses and randomized trials evaluating ultrasonic technology have demonstrated relative reductions in postoperative drainage volume and, in some reports, seroma formation; however, the magnitude and consistency of these effects vary considerably depending on study design, surgical workflow, and outcome definitions [18,26]. Importantly, most studies report seroma-related outcomes using relative effect measures such as odds ratios or risk ratios, which may obscure the absolute clinical burden of seroma and its downstream consequences. This limitation is further illustrated by large-scale evidence evaluating bipolar vessel-sealing systems. In a comprehensive systematic review and meta-analysis, Imran et al. examined the impact of LigaSure™ on postoperative outcomes following axillary lymph node dissection. Although significant reductions were observed in postoperative drainage volume (SMD −0.39) and drain duration (SMD −0.51), no statistically significant reduction in seroma incidence was demonstrated, with a pooled odds ratio close to unity and substantial interstudy heterogeneity [23]. These findings suggest that improvements in early lymphatic output do not necessarily translate into meaningful or durable reductions in clinically apparent seroma when energy devices are used as substitutes within otherwise conventional dissection techniques. In contrast, the Total Sealing Technique (TST) provides clear and clinically interpretable absolute reductions in both seroma incidence and the number of required aspiration procedures [5]. Rather than applying energy devices selectively, TST emphasizes the systematic and comprehensive sealing of lymphatic channels transected during axillary dissection, directly addressing the biological mechanisms underlying persistent lymphatic leakage. As a result, TST not only reduces the proportion of patients who develop postoperative seroma, but also substantially decreases the frequency of postoperative interventions required for seroma management. From both a clinical and health economic perspective, these absolute reductions are particularly meaningful, as seroma aspiration represents a common source of patient discomfort, repeated outpatient visits, and additional healthcare costs.

5.3. Long-Term Outcomes and Breast Cancer–Related Lymphedema

Long-term outcomes related to breast cancer–related lymphedema (BCRL) are infrequently reported in studies comparing Harmonic® devices with conventional electrocautery-based techniques [26,28]. Most randomized trials and meta-analyses evaluating ultrasonic energy focus predominantly on short-term postoperative endpoints, including drainage volume, seroma formation, and duration of drain placement, with follow-up periods typically limited to weeks or a few months after surgery. Consequently, the impact of Harmonic® technology on chronic lymphatic morbidity, including breast cancer–related lymphedema (BCRL), remains insufficiently characterized, as most available studies focus on short-term postoperative endpoints and lack extended follow-up. A similar limitation is observed in the literature evaluating bipolar vessel-sealing systems. In the most comprehensive systematic review and meta-analysis to date, Imran et al. demonstrated that LigaSure™ significantly reduces postoperative lymphorrhea, drain duration, and length of hospital stay compared with conventional techniques; however, no significant benefit was observed with respect to seroma-related outcomes, and long-term complications such as BCRL were not assessed [23]. These findings highlight a critical gap in the existing literature, wherein improvements in early postoperative parameters cannot be assumed to translate into durable reductions in long-term lymphatic morbidity. This evidence gap is particularly relevant given that BCRL is a delayed and progressive condition that may manifest months to years after axillary lymph node dissection. The absence of standardized long-term follow-up and consistent BCRL reporting in studies centered on energy device substitution constrains meaningful comparisons of sustained

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lymphatic outcomes and limits conclusions regarding true long-term benefit [26]. In contrast, the Total Sealing Technique (TST) directly addresses this unmet need by demonstrating a sustained and clinically meaningful reduction in BCRL incidence during long-term follow-up [10]. These data suggest that durable preservation of lymphatic function depends less on the specific energy modality employed and more on the comprehensiveness and consistency of lymphatic sealing achieved during the initial axillary dissection. Collectively, this distinction underscores the importance of technique-driven rather than device-driven innovation in mitigating long-term lymphatic morbidity after breast cancer surgery.

6. Health Economic Impact and Value-Based Surgical Care

6.1. Conceptual Framework for Economic Evaluation in ALND

Economic evaluation of surgical innovation requires consideration of costs and benefits across the full continuum of care. Time-Driven Activity-Based Costing and early health technology assessment frameworks emphasize the importance of capturing costs beyond the index procedure, including downstream resource utilization and long-term outcomes [29,30]. In the context of axillary lymph node dissection (ALND), costs can be broadly categorized into immediate inpatient costs, short-term outpatient costs, and long-term lifetime costs related to chronic morbidity, such as breast cancer–related lymphedema (BCRL), which has been shown to substantially increase healthcare utilization and expenditures over time [6,31]. However, traditional evaluations of surgical devices have often focused narrowly on operative time or disposable costs, while neglecting downstream clinical and economic consequences that may far outweigh initial expenditures [32]. Against this backdrop, the Total Sealing Technique (TST) provides a paradigm through which surgical technique can be assessed not merely as a technical choice, but as a determinant of long-term healthcare value [10].

6.2. Immediate Inpatient Costs: Length of Stay and Resource Utilization

Postoperative length of hospital stay (LOS) remains one of the most significant drivers of inpatient costs after breast cancer surgery [33]. After ALND, delayed functional recovery and readiness for discharge are commonly associated with persistent drainage, postoperative pain, restricted shoulder mobility, and early postoperative complications [34,35]. McManus et al. estimated the average daily cost of postoperative inpatient care following breast-conserving surgery with ALND at USD 2,454, reflecting hospital facility and nursing costs alone, exclusive of professional fees[2]. By markedly reducing lymphatic leakage and enabling earlier drain removal, TST directly addresses these key determinants, resulting in a 3.7-day shorter postoperative hospital stay compared with conventional techniques. Based on reported per diem costs, this reduction corresponds to an estimated inpatient cost savings of approximately USD 9,078 per patient. From a hospital management perspective, shorter LOS reduces nursing workload, medication utilization, laboratory testing, and the risk of nosocomial complications, while simultaneously improving bed turnover and effective capacity, particularly in high-volume cancer centers [36,37].

6.3. Short-Term Outpatient Costs: Seroma Management and Follow-Up Care

Seroma formation is a frequent cause of unplanned outpatient visits following ALND, often necessitating repeated clinic encounters and aspiration procedures [38,39]. Each aspiration encounter incurs direct medical costs as well as indirect costs related to patient travel, time off work, and caregiver burden. Published cost analyses indicate that a single seroma aspiration is associated with direct medical costs of approximately USD 370 per procedure, with reported estimates ranging from USD 200 to 500 per event [40–42]. Patients who develop postoperative seroma typically require an average of 2–4 aspiration procedures, resulting in cumulative outpatient costs of approximately USD 400–2,000 per affected patient [39]. By significantly reducing both seroma incidence and the number

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of required aspirations, TST translates these clinical benefits into immediate outpatient cost savings of approximately USD 400–1,000 per patient, even under conservative per-procedure cost assumptions [5,39,42]. At the population level, these per-patient savings may yield substantial reductions in healthcare expenditure, particularly in high-volume centers performing ALND. Importantly, these estimates reflect only direct medical costs and likely underestimate the total economic benefit, as indirect costs are not captured.

6.4. Long-Term Lifetime Costs: Prevention of Breast Cancer–Related Lymphedema

Breast cancer–related lymphedema (BCRL) represents one of the most consequential long-term economic burdens associated with ALND. Population-based analyses have demonstrated that BCRL is associated with sustained increases in healthcare utilization and medical expenditures over time [6]. Systematic reviews confirm that these costs persist across multiple domains of care, reflecting the chronic and progressive nature of the condition [43]. Management of BCRL is lifelong and typically involves compression therapy, physical therapy, repeated outpatient surveillance, and, in selected cases, surgical intervention, with costs increasing in parallel with disease severity and chronicity [2,44]. Beyond direct medical costs, BCRL is associated with substantial indirect economic consequences, including reduced productivity, disability, and psychosocial burden [45–47]. Cost analyses have shown that the development of BCRL is associated with excess direct medical expenditures of approximately USD 14,000–15,000 per affected patient within the first two years following breast cancer treatment, with costs continuing to accrue thereafter [6]. By reducing BCRL incidence from 22.2% to 2.9%, TST yields an absolute risk reduction of 19.3%, corresponding to an expected direct medical cost savings of approximately USD 2,700–2,900 per patient during the initial two-year period when calculated on an expected-value basis. Expressed alternatively, this represents an approximately 87% relative reduction in expected BCRL-related costs. Collectively, these findings underscore the economic value of preventive surgical strategies implemented at the time of initial axillary surgery.

6.5. Integration with Value-Based Healthcare Models

Value-based healthcare emphasizes outcomes that matter to patients relative to costs incurred. In breast cancer surgery, these outcomes include oncological control, functional preservation, quality of life, and survivorship. TST aligns closely with value-based care principles by improving short-term recovery while simultaneously mitigating long-term morbidity [48]. From a policy perspective, technique-centered approaches such as TST may contribute to more sustainable cancer care by reducing long-term demand for healthcare resources, particularly as health systems face increasing pressure to balance cost containment with high-quality care [2,48].

7. Limitations, Generalizability, and Future Research Directions

7.1. Limitations of the Current Evidence

While the available data on the Total Sealing Technique (TST) are compelling, several important limitations warrant careful consideration. First, the majority of studies evaluating TST to date have been conducted at single institutions with relatively limited sample sizes, raising the possibility of center-specific effects related to surgeon expertise, institutional protocols, or perioperative management pathways. Although the magnitude and internal consistency of the observed benefits—particularly with respect to lymphatic complications—support a true technique-related effect, external validity would be strengthened by prospective multicenter studies conducted across diverse practice settings [47]. Second, comparisons between TST and other energy-based devices, including Harmonic® and bipolar vessel-sealing systems, are constrained by substantial heterogeneity in study design, patient populations, surgical workflows, and outcome definitions. As highlighted in recent systematic reviews and meta-analyses, including the comprehensive analysis by Imran et al., most

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device-focused studies prioritize short-term perioperative endpoints such as drainage volume, drain duration, seroma formation, and length of hospital stay, while long-term outcomes are rarely assessed in a standardized manner. Notably, even large-scale meta-analyses have not evaluated breast cancer–related lymphedema (BCRL) as an outcome, limiting conclusions regarding durable lymphatic preservation[28]. This limitation is particularly relevant given that BCRL is a delayed and progressive condition that may develop months to years after axillary lymph node dissection. The lack of long-term follow-up and inconsistent reporting of BCRL across studies evaluating energy device substitution hampers meaningful comparison of sustained lymphatic outcomes and may lead to overestimation of long-term benefit based solely on early postoperative improvements[2]. Finally, standardized definitions and reporting frameworks for lymphatic complications—including seroma, drainage duration, and BCRL—remain lacking across the literature. Adoption of uniform outcome measures, extended follow-up periods, and integration of patient-reported outcomes will be essential for future studies to accurately characterize the long-term clinical value of technique-centered innovations such as TST.

7.2. Generalizability and Implementation Considerations

The Total Sealing Technique (TST) is inherently adaptable to a wide range of clinical settings, as it relies on widely available bipolar vessel-sealing technology and can be incorporated into standard axillary lymph node dissection workflows without the need for additional operative steps or specialized microsurgical equipment. This feature distinguishes TST from other preventive strategies that require advanced infrastructure or prolonged operative time, thereby enhancing its potential generalizability across institutions with varying resource levels. Nevertheless, successful implementation of TST depends critically on strict adherence to its underlying principles, particularly the systematic and comprehensive sealing of all lymphatic and vascular structures encountered during axillary dissection. Partial adoption or hybrid approaches—such as combining bipolar sealing for selected structures with monopolar electrocautery for general dissection—may compromise the intended benefits by allowing residual lymphatic leakage and collateral thermal injury [10]. As such, the effectiveness of TST is contingent not merely on device availability, but on consistent execution of the technique as a unified surgical strategy. To facilitate broader adoption and reproducibility, training and dissemination efforts should emphasize technique standardization rather than device familiarity alone. Structured educational initiatives, including stepwise operative protocols, video-based instruction, and supervised implementation during early experience, may help reduce variability in practice and optimize outcomes. By prioritizing uniform application of its core principles, TST can be reliably implemented across diverse practice environments, thereby maximizing its potential impact on postoperative outcomes and long-term lymphatic morbidity.

7.3. Future Research Directions

Future investigations should prioritize prospective, multicenter trials designed to compare the Total Sealing Technique (TST) with other contemporary approaches to axillary lymph node dissection, including Harmonic®-based techniques and emerging lymphatic preservation strategies. Such studies would enhance external validity and allow evaluation of TST across diverse patient populations, institutional practices, and healthcare systems. To more fully capture the clinical value of TST, future trials should incorporate patient-reported outcomes, quality-of-life measures, and standardized long-term endpoints, particularly the incidence and severity of breast cancer–related lymphedema (BCRL). In addition, formal cost-effectiveness and budget impact analyses are warranted to quantify the economic implications of TST relative to device-based and microsurgical alternatives, thereby informing value-based decision-making at both institutional and policy levels. In parallel, further investigation into the biological mechanisms underlying the reduction in BCRL observed with TST is needed. A plausible mechanistic hypothesis is that, compared with monopolar electrocautery, TST results in reduced lateral thermal spread and less collateral injury to perilymphatic tissues that are critical for preserving residual lymphatic function. However, direct

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validation of this hypothesis will require dedicated preclinical studies, including controlled animal experiments and detailed histopathological analyses, to systematically characterize tissue-level thermal injury, inflammatory response, and lymphatic integrity following different surgical energy modalities. Elucidation of these mechanisms would not only strengthen the biological rationale for TST but also guide further refinement of surgical techniques aimed at durable lymphatic preservation.

8. Educational and Training Implications

8.1. Standardization of Axillary Surgery

One of the most significant challenges in improving outcomes after axillary lymph node dissection (ALND) is substantial inter-surgeon variability. Differences in operative technique, selection and application of energy devices, and interpretation of dissection planes contribute to heterogeneity in postoperative outcomes, including lymphatic complications. The Total Sealing Technique (TST) directly addresses this challenge by providing a standardized, technique-centered framework that emphasizes reproducible operative steps and clearly defined intraoperative endpoints [5,10]. TST reduces reliance on subjective judgment and minimizes unwarranted technical variation between surgeons by prioritizing the comprehensive and systematic sealing of all tissues **on the cutting line** along the intended dissection plane. This structured approach facilitates consistent execution of axillary dissection across operators with differing levels of experience. By codifying the principles of comprehensive sealing into a clear sequence of seal–divide–advance, TST can function as an effective teaching paradigm for surgical trainees. This stepwise workflow provides trainees with an intuitive operative algorithm that may shorten the learning curve, improve procedural consistency, and enhance reproducibility of outcomes across surgeons and institutions [5,10].

8.2. Implications for Surgical Education

Incorporation of the Total Sealing Technique into surgical training curricula has the potential to improve long-term patient outcomes by instilling best practices early in a surgeon's career. Beyond its demonstrated clinical advantages, TST-based axillary dissection offers substantial educational value by promoting deliberate, anatomy-driven surgical decision-making. Training in this technique encourages trainees to develop a comprehensive three-dimensional understanding of axillary anatomy, including accurate identification of dissection planes and reliable differentiation between axillary adipose tissue and overlying subcutaneous fat. TST-based education also emphasizes principles of optimal operative field development, such as maintaining broad, planar exposure of the surgical field rather than focal traction, which facilitates precise and atraumatic dissection. In particular, when vascular structures are divided using sealing alone without ligation, trainees must learn to avoid sealing under tension. Instead, vessels should be returned to a relaxed, anatomically neutral state before performing double sealing followed by controlled division, reinforcing safe energy application and tissue handling principles. These deliberate steps provide repeated opportunities to reinforce fundamental surgical concepts, including respect for tissue biomechanics, appropriate use of energy devices, and prevention of collateral thermal injury. Simulation-based training modules and structured video-based education may further enhance dissemination of these principles and promote uniform adoption across institutions. Importantly, by emphasizing surgical technique and intraoperative judgment rather than reliance on a specific device, TST-oriented training fosters critical thinking, adaptability, and durable skill acquisition among trainees, supporting high-quality axillary surgery across diverse clinical settings.

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9. Global and Health Policy Perspectives

9.1. Variations in Practice Patterns

International variations in breast cancer surgery reflect differences in healthcare systems, reimbursement structures, and cultural expectations surrounding perioperative care. Comparative health services research has consistently demonstrated substantial cross-national variation in hospital utilization and postoperative length of stay for surgical care, including cancer surgery, even after adjustment for case mix and clinical outcomes [49]. In the context of axillary lymph node dissection (ALND), postoperative length of hospital stay varies widely, ranging from same-day discharge or short-stay pathways in some Western centers to prolonged hospitalization in other regions where traditional perioperative management remains common [50,51]. Shorter hospital stays, often achieved through enhanced recovery pathways and streamlined perioperative care, have been associated with reduced resource utilization without compromising short-term surgical outcomes [52]. Techniques that reliably reduce postoperative morbidity and facilitate earlier readiness for discharge may therefore confer disproportionate benefits in healthcare systems with longer baseline lengths of stay.

9.2. Implications for Resource-Limited Settings

In resource-limited settings, access to advanced microsurgical techniques for lymphedema prevention is frequently restricted. Global disparities in surgical capacity have been well documented, with shortages of specialized equipment, trained microsurgeons, and perioperative infrastructure limiting the feasibility of technically demanding procedures such as immediate lymphatic reconstruction in many regions of the world [53]. Even within high-income countries, access to microsurgical lymphedema prevention strategies is often concentrated in high-volume tertiary referral centers, resulting in geographic and institutional inequities in care delivery. These constraints are particularly relevant in health systems facing workforce shortages, cost containment pressures, and competing priorities for limited surgical resources. As a consequence, preventive strategies that rely on advanced microsurgical expertise may have limited scalability and global applicability, despite promising outcomes reported in specialized settings [54]. At first glance, the LigaSure™ Exact Dissector represents a nontrivial upfront expenditure, as it is a disposable device priced at approximately USD 670 per procedure. However, this initial cost must be interpreted within the broader context of downstream cost savings associated with the Total Sealing Technique (TST). As demonstrated in prior sections, TST is associated with marked reductions in postoperative length of hospital stay, fewer outpatient interventions for seroma management, and a substantially lower incidence of breast cancer–related lymphedema, each of which independently contributes to meaningful reductions in healthcare utilization and expenditure. From a health economic perspective, the incremental device cost of the LGSED is therefore more than offset by savings accrued across inpatient, outpatient, and long-term morbidity-related domains, resulting in a highly favorable cost–benefit profile. Importantly, these savings accrue early in the postoperative course and continue over time, making TST particularly attractive for healthcare systems operating under constrained budgets. Unlike microsurgical approaches, TST requires no additional infrastructure, specialized personnel, or prolonged operative time, further enhancing its feasibility and scalability across diverse practice environments. Taken together, these considerations indicate that TST represents not only a clinically effective strategy but also a highly cost-effective and pragmatic solution for improving axillary surgery outcomes in resource-limited settings. By coupling technical simplicity with durable reductions in postoperative morbidity, TST has the potential to advance more equitable, sustainable, and value-based breast cancer care on a global scale [10].

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10. Conclusions

Axillary lymph node dissection remains an essential component of breast cancer surgery for selected patients; however, its long-term value increasingly depends on the ability to minimize treatment-related morbidity. The Total Sealing Technique (TST) represents a technique-centered approach that prioritizes comprehensive lymphatic control, offering clinically meaningful reductions in postoperative complications and a substantial decrease in the incidence of breast cancer–related lymphedema. Beyond the direct clinical benefits observed in reduced lymphorrhea, seroma formation, and shortened hospital stay, TST confers quantifiable and immediate economic advantages across multiple phases of care. By shortening postoperative length of stay by 3.7 days, TST is associated with an estimated per-patient inpatient cost reduction of approximately USD 9,078. In addition, reduction in seroma aspiration frequency from 4.6 to 1.8 procedures per patient translates into immediate outpatient cost savings of approximately USD 400–1,000. Importantly, by suppressing the development of breast cancer–related lymphedema, TST further yields an expected reduction in direct medical costs of approximately USD 2,700–2,900 per patient within the first two years after surgery, even under conservative cost assumptions. Taken together, these effects demonstrate that the economic value of TST extends well beyond short-term perioperative metrics. By intervening at the time of initial surgery and minimizing lymphatic injury at its source, TST addresses the most consequential long-term complication of axillary surgery—breast cancer–related lymphedema—through a preventive strategy that is biologically rational, clinically effective, and economically meaningful. Importantly, the value of TST should be interpreted within the broader context of contemporary breast cancer care, which increasingly prioritizes survivorship, quality of life, and sustainability of healthcare systems. As systemic therapies and radiotherapy continue to improve oncological outcomes, the relative importance of minimizing treatment-related morbidity becomes ever greater. Surgical techniques that reduce long-term harm without compromising oncological safety are therefore integral to modern multidisciplinary cancer care. While further multicenter validation and formal cost-effectiveness analyses are warranted, the current body of evidence supports TST as a reproducible, scalable, and value-based approach to axillary surgery. Wider adoption of this technique, coupled with ongoing refinement and integration with complementary preventive strategies, has the potential to redefine quality benchmarks for axillary lymph node dissection in breast cancer.

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Abbreviations

The following abbreviations are used in this manuscript:

ALND	Axillary lymph node dissection
BCRL	Breast cancer-related lymphedema
SLNB	Sentinel lymph node biopsy
TST	Total sealing technique
CONV	Conventional electrocautery
ILR	Immediate lymphatic reconstruction
LGSED	LigaSure™ Exact Dissector

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References

1. Kim, J.; Harper, A.; McCormack, V.; Sung, H.; Houssami, N.; Morgan, E.; Mutebi, M.; Garvey, G.; Soerjomataram, I.; Fidler-Benaoudia, M.M. Global patterns and trends in breast cancer incidence and mortality across 185 countries. *Nat Med*. **2025**, *31*, 1154-1162.
2. DiSipio, T.; Rye, S.; Newman, B.; Hayes, S. Incidence of unilateral arm lymphoedema after breast cancer: a systematic review and meta-analysis. *Lancet Oncol*. **2013**, *14*, 500-515.
3. Naoum, G.E.; Roberts, S.; Brunelle, C.L.; Shui, A.M.; Salama, L.; Daniell, K.; Gillespie, T.; Bucci, L.; Smith, B.L.; Ho, A.Y.; et al. Quantifying the Impact of Axillary Surgery and Nodal Irradiation on Breast Cancer-Related Lymphedema and Local Tumor Control: Long-Term Results From a Prospective Screening Trial. *J Clin Oncol*. **2020**, *38*, 3430-3438.
4. McLaughlin, S.A.; Brunelle, C.L.; Taghian, A. Breast Cancer-Related Lymphedema: Risk Factors, Screening, Management, and the Impact of Locoregional Treatment. *J Clin Oncol*. **2020**, *38*, 2341-2350.
5. Ikeda, N.; Akahori, T.; Yokotani, T.; Fujii, T.; Sho, M. Total Sealing Technique (TST) with a bipolar vessel sealing system reduces lymphorrhea and seroma formation for axillary lymph node dissection in primary breast cancer. *Surg Open Sci*. **2024**, *19*, 1-7.
6. Shih, Y.C.; Xu, Y.; Cormier, J.N.; Giordano, S.; Ridner, S.H.; Buchholz, T.A.; Perkins, G.H.; Elting, L.S. Incidence, treatment costs, and complications of lymphedema after breast cancer among women of working age: a 2-year follow-up study. *J Clin Oncol*. **2009**, *27*, 2007-2014.
7. Sutton, P.A.; Awad, S.; Perkins, A.C.; Lobo, D.N. Comparison of lateral thermal spread using monopolar and bipolar diathermy, the Harmonic Scalpel and the Ligasure. *Br J Surg*. **2010**, *97*, 428-433.
8. Seki, T.; Hayashida, T.; Takahashi, M.; Jinno, H.; Kitagawa, Y. A randomized controlled study comparing a vessel sealing system with the conventional technique in axillary lymph node dissection for primary breast cancer. *Springerplus*. **2016**, *5*, 1004.
9. Nespoli, L.; Antolini, L.; Stucchi, C.; Nespoli, A.; Valsecchi, M.G.; Gianotti, L. Axillary lymphadenectomy for breast cancer. A randomized controlled trial comparing a bipolar vessel sealing system to the conventional technique. *Breast*. **2012**, *21*, 739-745.
10. Ikeda, N.; Nagata, T.; Umemura, T.; Watanabe, M. Total Sealing Technique: A Preliminary Study on a Novel Surgical Approach That Significantly Reduces the Incidence of Upper Extremity Lymphedema Following Axillary Dissection in Patients with Breast Cancer. *Cancers (Basel)*. **2025**, *17*.
11. Novitsky, Y.W.; Rosen, M.J.; Harrell, A.G.; Sing, R.F.; Kercher, K.W.; Heniford, B.T. Evaluation of the efficacy of the electrosurgical bipolar vessel sealer (LigaSure) devices in sealing lymphatic vessels. *Surg Innov*. **2005**, *12*, 155-160.
12. Box, G.N.; Lee, H.J.; Abraham, J.B.; Deane, L.A.; Elchico, E.R.; Abdelshehid, C.A.; Alipanah, R.; Taylor, M.B.; Andrade, L.; Edwards, R.A.; et al. Comparative study of in vivo lymphatic sealing capability of the porcine thoracic duct using laparoscopic dissection devices. *J Urol*. **2009**, *181*, 387-391.
13. Kuroi, K.; Shimozuma, K.; Taguchi, T.; Imai, H.; Yamashiro, H.; Ohsumi, S.; Saito, S. Evidence-based risk factors for seroma formation in breast surgery. *Jpn J Clin Oncol*. **2006**, *36*, 197-206.
14. van Bemmel, A.J.; van de Velde, C.J.; Schmitz, R.F.; Liefers, G.J. Prevention of seroma formation after axillary dissection in breast cancer: a systematic review. *Eur J Surg Oncol*. **2011**, *37*, 829-835.
15. Ebner, F.; Friedl, T.W.P.; de Gregorio, A.; Lato, K.; Bekes, I.; Janni, W.; de Gregorio, N. Seroma in breast surgery: all the surgeons fault? *Arch Gynecol Obstet*. **2018**, *298*, 951-959.
16. Porter, K.A.; O'Connor, S.; Rimm, E.; Lopez, M. Electrocautery as a factor in seroma formation following mastectomy. *Am J Surg*. **1998**, *176*, 8-11.
17. Campbell, P.A.; Cresswell, A.B.; Frank, T.G.; Cuschieri, A. Real-time thermography during energized vessel sealing and dissection. *Surg Endosc*. **2003**, *17*, 1640-1645.
18. Yilmaz, K.B.; Dogan, L.; Nalbant, H.; Akinci, M.; Karaman, N.; Ozaslan, C.; Kulacoglu, H. Comparing scalpel, electrocautery and ultrasonic dissector effects: the impact on wound complications and pro-inflammatory cytokine levels in wound fluid from mastectomy patients. *J Breast Cancer*. **2011**, *14*, 58-63.
19. Thompson, M.; Korourian, S.; Henry-Tillman, R.; Adkins, L.; Mumford, S.; Westbrook, K.C.; Klimberg, V.S. Axillary reverse mapping (ARM): a new concept to identify and enhance lymphatic preservation. *Ann Surg Oncol*. **2007**, *14*, 1890-1895.

 doi:10.20944/preprints202601.0577.v1

20. Kakos, G.S.; James, A.G. The use of cautery in "bloodless" radical mastectomy. *Cancer*. **1970**, *26*, 666-668.
21. Miller, E.; Paull, D.E.; Morrissey, K.; Cortese, A.; Nowak, E. Scalpel versus electrocautery in modified radical mastectomy. *Am Surg*. **1988**, *54*, 284-286.
22. Birkmeyer, J.D.; Finks, J.F.; O'Reilly, A.; Oerline, M.; Carlin, A.M.; Nunn, A.R.; Dimick, J.; Banerjee, M.; Birkmeyer, N.J. Surgical skill and complication rates after bariatric surgery. *N Engl J Med*. **2013**, *369*, 1434-1442.
23. Imran, M.; Ali, M.; Umar, T.P.; Ali, S.; Khalil, S.; Irfan, H.; Muhammad, A.; Javed, A.; Shahzadi, F.; Ara, S.; et al. Efficacy and Safety of LigaSure in Breast Surgery With Axillary Lymph Node Dissection in Patients With Breast Cancer: A Systematic Review and Meta-Analysis. *Surg Innov*. **2025**, *32*, 155-164.
24. Shemen, L. Thyroidectomy using the harmonic scalpel: analysis of 105 consecutive cases. *Otolaryngol Head Neck Surg*. **2002**, *127*, 284-288.
25. Ecker, T.; Carvalho, A.L.; Choe, J.H.; Walosek, G.; Preuss, K.J. Hemostasis in thyroid surgery: harmonic scalpel versus other techniques--a meta-analysis. *Otolaryngol Head Neck Surg*. **2010**, *143*, 17-25.
26. Huang, J.; Yu, Y.; Wei, C.; Qin, Q.; Mo, Q.; Yang, W. Harmonic Scalpel versus Electrocautery Dissection in Modified Radical Mastectomy for Breast Cancer: A Meta-Analysis. *PLoS One*. **2015**, *10*, e0142271.
27. Khan, S.; Khan, S.; Chawla, T.; Murtaza, G. Harmonic scalpel versus electrocautery dissection in modified radical mastectomy: a randomized controlled trial. *Ann Surg Oncol*. **2014**, *21*, 808-814.
28. Cheng, H.; Clymer, J.W.; Ferko, N.C.; Patel, L.; Soleas, I.M.; Cameron, C.G.; Hinoul, P. A systematic review and meta-analysis of Harmonic technology compared with conventional techniques in mastectomy and breast-conserving surgery with lymphadenectomy for breast cancer. *Breast Cancer (Dove Med Press)*. **2016**, *8*, 125-140.
29. Najjar, P.A.; Strickland, M.; Kaplan, R.S. Time-Driven Activity-Based Costing for Surgical Episodes. *JAMA Surg*. **2017**, *152*, 96-97.
30. MJ, I.J.; Koffijberg, H.; Fenwick, E.; Krahn, M. Emerging Use of Early Health Technology Assessment in Medical Product Development: A Scoping Review of the Literature. *Pharmacoeconomics*. **2017**, *35*, 727-740.
31. Johnson, A.R.; Asban, A.; Granoff, M.D.; Kang, C.O.; Lee, B.T.; Chatterjee, A.; Singhal, D. Is Immediate Lymphatic Reconstruction Cost-effective? *Ann Surg*. **2021**, *274*, e581-e588.
32. Kirisits, A.; Redekop, W.K. The economic evaluation of medical devices: challenges ahead. *Appl Health Econ Health Policy*. **2013**, *11*, 15-26.
33. Bucknor, A.; Chattha, A.; Ultee, K.; Wu, W.; Kamali, P.; Bletsis, P.; Chen, A.; Lee, B.T.; Cronin, C.; Lin, S.J. The financial impact and drivers of hospital charges in contralateral prophylactic mastectomy and reconstruction: a Nationwide Inpatient Sample hospital analysis. *Breast Cancer Res Treat*. **2017**, *165*, 301-310.
34. Baas-Vrancken Peeters, M.J.; Kluit, A.B.; Merkus, J.W.; Breslau, P.J. Short versus long-term postoperative drainage of the axilla after axillary lymph node dissection. A prospective randomized study. *Breast Cancer Res Treat*. **2005**, *93*, 271-275.
35. Devoogdt, N.; Van Kampen, M.; Christiaens, M.R.; Troosters, T.; Piot, W.; Beets, N.; Nys, S.; Gosselink, R. Short- and long-term recovery of upper limb function after axillary lymph node dissection. *Eur J Cancer Care (Engl)*. **2011**, *20*, 77-86.
36. McManus, S.A.; Topp, D.A.; Hopkins, C. Advantages of outpatient breast surgery. *Am Surg*. **1994**, *60*, 967-970.
37. Siddique, S.M.; Tipton, K.; Leas, B.; Greysen, S.R.; Mull, N.K.; Lane-Fall, M.; McShea, K.; Tsou, A.Y. Interventions to Reduce Hospital Length of Stay in High-risk Populations: A Systematic Review. *JAMA Netw Open*. **2021**, *4*, e2125846.
38. Andeweg, C.S.; Schriek, M.J.; Heisterkamp, J.; Roukema, J.A. Seroma formation in two cohorts after axillary lymph node dissection in breast cancer surgery: does timing of drain removal matter? *Breast J*. **2011**, *17*, 359-364.
39. Srivastava, V.; Basu, S.; Shukla, V.K. Seroma formation after breast cancer surgery: what we have learned in the last two decades. *J Breast Cancer*. **2012**, *15*, 373-380.
40. Tran, B.N.N.; Fadayomi, A.; Lin, S.J.; Singhal, D.; Lee, B.T. Cost analysis of postmastectomy reconstruction: A comparison of two staged implant reconstruction using tissue expander and acellular dermal matrix with abdominal-based perforator free flaps. *J Surg Oncol*. **2017**, *116*, 439-447.

 doi:10.20944/preprints202601.0577.v1

41. Lembo, F.; Cecchino, L.R.; Parisi, D.; Portincasa, A. Reduction of seroma and improvement of quality of life after early drain removal in immediate breast reconstruction with tissue expander. Preliminary report from a randomized controlled study. *J Plast Reconstr Aesthet Surg*. **2021**, *74*, 2565-2572.
42. de Blacam, C.; Momoh, A.O.; Colakoglu, S.; Slavin, S.A.; Tobias, A.M.; Lee, B.T. Cost analysis of implant-based breast reconstruction with acellular dermal matrix. *Ann Plast Surg*. **2012**, *69*, 516-520.
43. De Vrieze, T.; Nevelsteen, I.; Thomis, S.; De Groef, A.; Tjalma, W.A.A.; Gebruers, N.; Devoogdt, N. What are the economic burden and costs associated with the treatment of breast cancer-related lymphoedema? A systematic review. *Support Care Cancer*. **2020**, *28*, 439-449.
44. Stout, N.L.; Pfalzer, L.A.; Springer, B.; Levy, E.; McGarvey, C.L.; Danoff, J.V.; Gerber, L.H.; Soballe, P.W. Breast cancer-related lymphedema: comparing direct costs of a prospective surveillance model and a traditional model of care. *Phys Ther*. **2012**, *92*, 152-163.
45. Dean, L.T.; Moss, S.L.; Ransome, Y.; Frasso-Jaramillo, L.; Zhang, Y.; Visvanathan, K.; Nicholas, L.H.; Schmitz, K.H. "It still affects our economic situation": long-term economic burden of breast cancer and lymphedema. *Support Care Cancer*. **2019**, *27*, 1697-1708.
46. Boyages, J.; Xu, Y.; Kalfa, S.; Koelmeyer, L.; Parkinson, B.; Mackie, H.; Viveros, H.; Gollan, P.; Taksa, L. Financial cost of lymphedema borne by women with breast cancer. *Psychooncology*. **2017**, *26*, 849-855.
47. Hayes, S.C.; Janda, M.; Cornish, B.; Battistutta, D.; Newman, B. Lymphedema after breast cancer: incidence, risk factors, and effect on upper body function. *J Clin Oncol*. **2008**, *26*, 3536-3542.
48. Porter, M.E. What is value in health care? *N Engl J Med*. **2010**, *363*, 2477-2481.
49. Zhang, Y.; Baik, S.H.; Fendrick, A.M.; Baicker, K. Comparing local and regional variation in health care spending. *N Engl J Med*. **2012**, *367*, 1724-1731.
50. Kehlet, H. Fast-track surgery-an update on physiological care principles to enhance recovery. *Langenbecks Arch Surg*. **2011**, *396*, 585-590.
51. Arsalani-Zadeh, R.; ElFadl, D.; Yassin, N.; MacFie, J. Evidence-based review of enhancing postoperative recovery after breast surgery. *Br J Surg*. **2011**, *98*, 181-196.
52. Sauro, K.M.; Smith, C.; Ibadin, S.; Thomas, A.; Ganshorn, H.; Bakunda, L.; Bajgain, B.; Bisch, S.P.; Nelson, G. Enhanced Recovery After Surgery Guidelines and Hospital Length of Stay, Readmission, Complications, and Mortality: A Meta-Analysis of Randomized Clinical Trials. *JAMA Netw Open*. **2024**, *7*, e2417310.
53. Meara, J.G.; Leather, A.J.; Hagander, L.; Alkire, B.C.; Alonso, N.; Ameh, E.A.; Bickler, S.W.; Conteh, L.; Dare, A.J.; Davies, J.; et al. Global Surgery 2030: evidence and solutions for achieving health, welfare, and economic development. Lancet. 2015,
54. Johnson, A.R.; Singhal, D. Immediate lymphatic reconstruction. *J Surg Oncol*. **2018**, *118*, 750-757.