Keynote Lecture Series

Transition from multiportal video-assisted thoracic surgery to uniportal video-assisted thoracic surgery… and evolution to uniportal robotic-assisted thoracic surgery?

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The greatest disruptive innovation in lung cancer surgery in modern times has been the switch from open thoracotomy to video-assisted thoracic surgery (VATS). More recently, the transition from multiportal VATS (MVATS) to uniportal VATS (UVATS) has represented another mini-advance in reducing surgical access trauma. In the search for the next breakthrough in lung cancer surgery, a number of promising candidates have emerged, including screening, sublobar resections, 3D technology, enhanced peri-operative care pathways, ablative therapy and multi-modality management. However, could the way forwards be simply a further minimization of surgical access trauma, and could this be achieved by uniportal robotic surgery? Emergence of a 'winning' candidate will depend on a systematic evaluation of the evidence for the benefits and costs of each.

Keywords: Video-assisted thoracic surgery (VATS); uniportal, robotic; thoracic surgery

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The establishment of multiportal video-assisted thoracic surgery (MVATS)

Every so often in medicine, a disruptive innovation appears that completely overturns existing clinical practices. The development of the cardiopulmonary bypass systems in the 1950s gave birth to modern cardiac surgery (1). The discovery of *Helicobacter pylori* and its link to peptic ulcer disease revolutionized how gastric disease is treated, and won a Nobel Prize for Dr. Barry Marshall (2). For thoracic surgeons, the discovery of Streptomycin in the 1940s began the conversion of tuberculosis from a surgically managed disease to a primarily non-surgical pathology (3).

In recent times, the closest equivalent in thoracic surgery to a similarly disruptive innovation has undoubtedly been the advent of video-assisted thoracic surgery (VATS) (4-6). Almost all general thoracic surgical procedures had traditionally been performed via an open thoracotomy—recognized as one of the most painful incisions in any branch of surgery. By using a video-thoracoscope to replace the surgeon's eyes, and ported instruments to replace the surgeon's hands, VATS allowed the same operations to be performed with significantly less access trauma. The VATS approach met considerable resistance from the thoracic surgical community when it was first developed in the 1990s, with many criticizing it as a gimmick that compromised surgery. It was not until the early years of the 21st Century that it gradually became established as not only an alternative to thoracotomy, but the approach of choice for major operations such as lung cancer resection (7).

The story of how VATS rose from a radical upstart, to become the mainstream technique has been covered in detail in other articles by this author (4-6). Essentially, it acquired such status by the diligent work of VATS surgeons around the world accumulating real-world clinical evidence proving its value step-by-step (8,9). These steps can be crudely summarized as follows (although overlap in this timeline exists):

(I) Infancy: case reports and case summaries from the early 1990s gradually demonstrated the safety and feasibility of VATS for an ever-increasing range of operations;

(II) Childhood: early comparative studies from the mid-1990s demonstrated the benefit of VATS over thoracotomy using crude outcome measures (subject to more confounding variables), such as pain and lengths of stay;

(III) Adolescence: more sophisticated studies confirmed the benefit of VATS by using objective, quantifiable outcome measures such as physical function and measurements of cytokines and inflammatory markers;

(IV) Adulthood: systematic reviews and meta-analyses of accumulated survival data from the early 2000s proved that VATS gave equivalent—if not marginally superior—treatment efficacy to thoracotomy for lung cancer and other diseases.

Following these steps has proven to be essential for any new surgical technique or technology to supplant the previous 'gold standard' and become the modality of choice. For VATS, a couple of more recent randomized controlled trials have increased the level of evidence for the benefits of VATS, reinforcing the conclusions already drawn from the above steps (10,11).

Looking back, no other single advance has so changed the landscape of thoracic surgery over the last thirty years as the rise of VATS (6). Patients' post-operative outcomes have improved dramatically, and so have their expectations. Alongside this, VATS has today become a core component in the training of any thoracic surgeon (12).

The transition to uniportal VATS (UVATS)

A by-product of the rise of VATS has been the realization that surgical access trauma matters greatly, and that any advances made to minimize that trauma or its harms may result in measurable improvements in patient outcomes. For example, the understanding that even VATS can leave patients with residual paresthesia has led to recognition of neuropathy as a distinct type of pain following thoracic surgery (resulting from pressure to the intercostal nerves during instrumentation between the ribs) (13,14). This in turn has led to the use of pharmacotherapy specifically aimed at treating such neuropathic paresthesia (15). The experimentation with different forms of nerve blockade (particularly paravertebral) and when to apply this (particularly pre-emptively) have also resulted in measurable reduction in post-VATS morbidity (16).

However, the most obvious inference from the rise of VATS is surely that if benefits are gained by reducing the surgical access trauma itself, then further reducing this access trauma must also further increase the benefits. Conventionally, VATS was performed using three or more ports, including one 'utility' port to allow retrieval of the resected tissue (9). To reduce the access trauma, the logical next step was to reduce the number of ports to just one—giving birth to the technique of single-port or UVATS. Via a single incision, the video-thoracoscope and all instruments are placed to perform surgery (17). By limiting trauma to a single intercostal space, and possibly by improved geometry with less torquing via the wound, it is in theory possible to reduce trauma even when compared to multiportal VATS.

The UVATS approach was first reported for simple procedures such as lung wedge resections and pneumothorax surgery (18,19). However, the biggest leap forward came in 2011 when Dr. Diego Gonzalez published the first report of a lobectomy performed via a UVATS approach (20). This was the first step in the infancy phase of UVATS' evidence accumulation. In the years since, Dr. Diego Gonzalez-Rivas and many others have gone on to report the successful use of UVATS for almost every type of thoracic operation (21-25). The safety and feasibility of the UVATS approach has been confirmed by the collected clinical experience reported from every continent on earth (26).

It has been reassuring to see that the progression of clinical evidence for UVATS has largely followed the steps outlined above for conventional MVATS (6,9). Direct comparative studies have gradually demonstrated that UVATS offers similar or better patient outcomes compared to MVATS using the usual assortment of crude outcome measures, with most studies showing a clear advantage for UVATS in terms of early post-operative pain (26,27). A recent study has also shown that UVATS results in less immuno-chemokine disturbance than MVATS, following the progression towards use of more objective outcome measures (28). A couple of meta-analyses have now suggested that treatment efficacy (in terms of lymph node dissection and mid-term survival) is similar with UVATS and MVATS (29,30). When UVATS was first introduced, it faced stiff criticism from traditionalists as did MVATS in the 1990s, with many claiming there was insufficient evidence for them to switch to UVATS. However, with this robust build-up of clinical evidence in the last decade, UVATS has now become increasingly established as a mainstream approach (6,8,9). A 2018 survey of thoracic surgeons in Europe already showed a significant and growing proportion of surgeons using UVATS for a variety of thoracic operations (31). The uptake of UVATS in China has been even faster, and is now the approach of choice in many centers (32). Today, UVATS is so ubiquitous that thoracic surgery journals and conferences worldwide no longer consider most simple articles about it novel enough for acceptance.

Notwithstanding the global interest in UVATS, it must still be acknowledged that UVATS is not the huge advance that conventional MVATS was. The improvement seen over MVATS is increasingly undeniable, but the actual magnitude of that improvement is not as great as that between MVATS versus open thoracotomy (26,27). The above evidence has helped establish the status of UVATS as a valid surgical approach, but cannot justify why it has become so popular. The surge in uptake of UVATS owes perhaps more to a more unorthodox element: the energy and sheer charisma of Dr. Diego Gonzalez-Rivas. No one who has met him can deny his fiercely infectious passion for UVATS, and his drive to teach the technique hands-on has taken him to over 120 countries around the world. The UVATS training course he established in Shanghai has now converted hundreds of thoracic surgeons to take up UVATS (33). It is impossible to separate the success of UVATS from the personal touch and relentless evangelical efforts of Dr. Diego Gonzalez-Rivas in sharing it with surgeons everywhere.

The next big thing?

Having experienced the success of conventional VATS and now UVATS, the world of thoracic surgery eagerly anticipates what the next breakthrough in this specialty may be. As said above, to achieve the status of the 'Next Big Thing', any innovation should have to demonstrate its safety, benefits over existing practices and treatment efficacy. The following are some candidates for this prized position.

Lung cancer screening

A number of recent studies in North America, Europe and Asia have now confirmed the value of low-dose computed tomography (LDCT) for screening lung cancer in asymptomatic individuals (34-36). Those found to have malignancy are discovered in a very early stage, and are hence potentially curable by surgery. No other innovation mentioned in this article has as great a potential to reduce the mortality of the leading cancer cause of death in the world (37). For thoracic surgeons, successful implementation of LDCT screening may lead to a greatly increased demand for surgery, and steer surgery towards more minimally invasive directions to deal with the smaller lesions being identified (37). However, significant obstacles remain: who pays for screening is unresolved; the ideal selection criteria for screening are undefined (and may vary between regions); the optimal management for screening-detected lesions is still controversial (debate over over-diagnosis versus under-treatment rages); and others (38).

Sublobar resection

The reporting of the long awaited JCOG0802 and CALGB 140503 trials have now cemented the position of sublobar resection as a viable operation for small, peripheral lung cancers (39,40). Sublobar resections promises to offer equal (maybe better) survival than traditional lobectomy whilst better preserving patient lung function (41). Once again, though, there are many questions that must be answered before sublobar resection can become a gold standard: whether the less-than-expected lung function preservation demonstrated in the above trials was can justify the switch to sublobar resection; whether wedge resection is necessarily inferior to segmentectomy (especially after CALGB 140503); whether different considerations apply for simple versus complex segmentectomies or single versus multiple segments resected; and others (42). Given that segmentectomies are seen as technically more challenging by many thoracic surgeons, the answers are awaited anxiously as they may affect training or re-training of skillsets.

Peri-operative: enhanced recovery after surgery (ERAS), drainology, tubeless strategies

It has been well-argued that the advantages of VATS may be attributable as much to improved peri-operative care as the minimizing of surgical access trauma. With good care to all details of pre-, intra- and post-operative management, it has been shown that patient outcomes similar to VATS can be achieved even with open thoracotomy (43). Today, the systematic approach to such peri-operative care has been termed ERAS, and this has fast become essential practice for thoracic surgeons (44). Elements include nutritional management, use of advanced anesthetic techniques, and meticulous prehabilitation and rehabilitation interventions (45,46). The management of chest drains—including consideration of tube selection, suction strategy, removal criteria and so on—is becoming a focus of study in its own right, called 'drainology' (47). However, there is such variation in practices and preferences between different centers around the world that it is highly unlikely that a single 'one-size-fits-all' ERAS or drainology solution will ever emerge as a universal standard. A small number of surgeons have even reported experience with VATS in spontaneously breathing or even fully awake patients, foregoing the potential harms of endotracheal intubation (48). However, there is a long way to go before the evidence for these approaches fulfills the steps noted above for establishing their role.

New technology for VATS: navigation, 3D, artificial intelligence (AI)

The surgical products industry has invested heavily in developing a range of technologies that may excite thoracic surgeons. These include: navigation systems for bronchoscopy and percutaneous interventions; 3D video imaging; 3D printing and virtual modelling of complex anatomy; AI for diagnosis and decision-making; next-generation robot systems for not only surgery but bronchoscopy; and others (49). Whilst these are all immediately mesmerizing, they all come with a cost in terms of initial capital outlay, maintenance fees, training costs and competition for limited operating theatre time. The value proposition (increase in outcomes divided by cost expenditure) may perhaps be disappointing given that the surgical outcomes today are rarely most limited by the factors these expensive technologies address. From an academic perspective, it has also proven difficult to find adequate outcome measures to scientifically prove any advantages of these technologies. For example, many papers reporting on the use of navigation or 3D imaging continue to rely on operation times, post-operative morbidity and lengths of stay as outcome measures (50). However, these crude outcome measures are obviously subject to multiple confounding variables, and 'improvements' in them cannot reliably be attributed to just that technology alone.

Ablative therapy

An area of technology that deserves a separate mention is the use of various ablative modalities to ablate intra-thoracic pathologies—including radio-frequency, microwave and cryo-ablation (51). These can variously be delivered surgically, endo-bronchially or percutaneously (51,52). They have the promise of achieving 'elimination' of the pathology without the patient having to undergo amputation of any body tissue. Ablation has the potential to be a game-changer: if successful, it can render resective surgery (i.e., VATS and sublobar resections) obsolete. However, to become so, it must also accumulate clinical evidence step-by-step in the same way as described for conventional VATS above, and at the time of this writing, such evidence is still scanty and accumulating at a slow rate. In the meantime, other possibly competitive treatment modalities are also being investigated, including stereotactic body radiation therapy (SBRT) and proton/photon beam therapy (53).

Multi-modality therapy

In the last few years, great advances have been made in the use of target therapy and immunotherapy for lung cancer. When used in conjunction with surgery and chemotherapy in an adjuvant setting, both third-generation tyrosine kinase inhibitor (TKI) and checkpoint inhibitor monoclonal antibody therapy have delivered very significant survival improvements (54,55). On one end of the scale, even some stage IB patients may benefit, meaning that thoracic surgeons need to become ever more aware of the need for genetic mutation testing even in early-stage lung cancer patients. At the other end of the scale, improvements for patients with stage IIIA disease are very dramatic, which may portend lowering of thresholds for surgery in such patients within multi-disciplinary tumor boards for selected patients. Emerging trial results suggest similarly promising outcomes with neoadjuvant immunotherapy also—although the costs in terms of increased surgical morbidity and pre-operative attrition (patients who do not subsequently receive surgery) remain to be fully clarified (56,57). Altogether, this new era of multi-modality therapy for lung cancer will transform thoracic surgery, obliging surgeons to work less in isolation and more in close collaboration with other tumor board specialists for almost every patient. The only thing preventing this from being the 'Next Big Thing' in thoracic surgery is that it is not a surgical innovation *per* *se*, and will affect the circumstances of the surgery rather than the practice of surgery itself.

An evolution to uniportal robot-assisted thoracic surgery (URATS)?

As seen above, there are many innovations around the practice of thoracic surgery in general—and lung cancer surgery in particular—that have potential to become the next breakthrough in the specialty. Each shows great promise for changing and improving thoracic surgery, but each also has potential factors delaying or preventing its emergence as a game-changer. That being the case, is it possible that the next major advance is simply more of the same? That is, following from the progress of open thoracotomy to conventional VATS to UVATS, perhaps the 'Next Big Thing' is simply a further minimizing of surgical access trauma.

There are broadly-speaking two approaches to how such surgical access trauma might be reduced further from UVATS. The first is to seek alternative sites for the single port in UVATS. It is recognized that much of the trauma from VATS is due to the aforementioned neuropathy at the intercostal nerves. It has therefore been hypothesized that avoiding the use of the intercostal space altogether for thoracic surgery should eliminate a significant component of post-operative pain and morbidity. To this end, intrepid surgeons from different parts of the world have variously reported the performance of UVATS via subxiphoid, subcostal, transcervical and even transumbilical incisions (58-60). The subxiphoid approach is now gaining acceptance as an alternative approach for thymic surgery (58). However, each has been reported to have particular technical difficulties, and the accumulated clinical evidence for each remains very limited for now. It seems unlikely that these will find the same success as UVATS given the technical challenges and the possibly minimal benefit over conventional VATS or UVATS.

The other, better developed approach to improve minimally invasive surgery is through the use of robotics. Robot-assisted thoracic surgery (RATS) is far from new, having been pioneered over twenty years ago (61). The potential advantages of RATS have been very well advertised over the years, including: 3D vision; dexterous, stable instrumentation; reduced torquing at the ports; better surgeon ergonomics; and so on. Over the years, as with UVATS, it has been demonstrated that almost any thoracic operation can be safely and feasibly performed using RATS (61). During these years, much clinical evidence has also accumulated proving the advantages of RATS over open thoracotomy (29). However, the accumulated evidence also has failed to demonstrate any distinct advantage of RATS over conventional MVATS—much less UVATS (29). Indeed, meta-analysis has instead shown that the only significant difference between RATS and MVATS is the cost, with the latter being much cheaper (29). Given the capital, maintenance and training costs, the value of RATS may be diminished for many centers. This may in part explain why UVATS uptake has overtaken RATS uptake around the world despite the ten-year head start of RATS.

The drawbacks of RATS in terms of value may be overcome by either reducing costs or by improving the outcomes. The former is already coming true as the monopoly of the only RATS system manufacturer is coming to an end, and alternative, cheaper RATS systems are now emerging on the marketplace. The latter may also be coming true as an intrepid handful of surgeons have begun to experiment with a URATS approach for various types of lung resections, using a single intercostal incision, without rib spreading (62-65). A robotic camera, robotic dissecting instruments and robotic staplers are used, without the need of a bedside assistant to handle any conventional VATS staplers and instruments (63,64). The potential advantage of this URATS approach is the combination of the best of both UVATS and conventional RATS. Conventional RATS uses 3 to 4 ports, which may explain why it is hard to demonstrate any benefit over MVATS. By performing RATS through only a single port, it is hypothesized that one may achieve the pinnacle of minimal access thoracic surgery.

At this point, it is important to remember that this potential remains a hypothesis. At the time of this writing, all that the world knows is that a very small number of surgeons have performed an unspecified number of URATS operations (62-64). To date, only one group has reported a series of 24 URATS lung resections without mortality (65). There is as yet no further consistent documentation of the overall safety of the approach. There is certainly no proof that any of the hypothesized advantages are true when compared to any other surgical technique. There is also a very long way to go, presumably, before any data is produced to show the treatment efficacy of the URATS technique. As has been emphasized above, for any new surgical innovation, it is imperative that all the steps of evidence accumulation are fulfilled before that innovation can be viewed as an acceptable practice—let alone an established or preferable one (6,9). In the absence of such evidence, URATS at present can only be viewed as a novel idea.

That is not to say that URATS may not become the 'Next Big Thing' in thoracic surgery in the future. History teaches that many of the standard practices that surgeons use today first started as eccentric new ideas. Time and diligent clinical research will tell the difference between a gimmick and a game-changer. It is essential that thoracic surgeons who are enthusiastic about URATS be patient when awaiting the evidence, and not rush to embrace any 'new' innovation until it has been proven safe and effective. It took years before VATS and then UVATS became established (4,8). By the same token, it behooves skeptics to also give URATS some time to develop, remembering that early critics of conventional VATS were also converted in the end. The evolution of thoracic surgery requires level heads and open minds.

Concluding thoughts

Surgeons are, amongst other things, products of science. Science itself has been defined as the "systematic pursuit of knowledge involving the recognition and formulation of a problem, the collection of data through observation and experiment, and the formulation and testing of hypotheses" (66). In thoracic surgery, daily clinical practice allows the attentive amongst us to recognize areas for improvement in our practice, and the intrepid amongst us to formulate hypothetical solutions. As noted in this article, such potential solutions in thoracic surgery include: lung cancer screening; sublobar resection; enhanced peri-operative care; new technologies; ablative therapy; multi-modality cancer therapy; and URATS. Should any one of these innovations break through and succeed, it can revolutionize the way we practice our craft to help patients. However, science mandates that these ideas each be rigorously tested and experimented on to separate the effective from the distracting. Science also requests that we give each hypothesis a fair chance to be tested before conclusions are reached. Whether URATS emerges as the next major disruptive innovation in thoracic surgery should be up to science to prove.

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Footnote

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