



En bloc resection of bladder tumors (ERBT) revisited 12 years after reintroduction: too good to be further ignored

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Abstract

En bloc resection of bladder tumors (ERBT) originally described in 1980 and adopted by few centers in the late 1990s has regained attention in the 2010s as a renaissance of a technique with high potential. The advent of new lasers indirectly lead to a better understanding of anatomical dissection from the experience in anatomical dissection in endoscopic enucleation of the prostate. 12 years after the reintroduction of ERBT evidence mounts that it is not only equivalent but better in some regards. However, ERBT still falls short with regard to wide adoption despite the striking technique inherent and reproducible features of accurate staging and specimen quality as requested by pathologist, as well and despite the high intraoperative safety and fast adoption of this technique even in early phase of training. The editorial walks the reader through the timeline of the renaissance speculating why there is a blockage between cognitive understanding and dissonance in surgical practice. The special issues presents the meta-analysis of surgical and oncological data on one hand and the level of understanding and power of this surgical technique in fields offsite oncological results in training achieving results almost right from the start after adoption. Unlike in earlier years reviewing the literature of ERBT in 2023, ERBT seems not only to be a viable alternative, but something one should turn towards no to underperform with regards to the endpoints achievable by ERBT in a critical disease like bladder cancer.

Sometimes, the small but subtle difference in the reception of ancient phrases of wisdom lies in the process of coining slogans that suit the author more than the fineness of human thought and action. The famous verse of Titus Maccius Plautus in his comedy *Truculentus* [1] is most often referred to as “Seeing is believing.” However, this was true for my name patron Saint Thomas the Apostle and for the impromptu convert to en bloc resection of bladder tumors (ERBT), Marek Babjuk, visiting me at Hanover Medical School (MHH) 2013 being exposed to ERBT surgery for the first time. However, the topos of cognition and action has been the subject of epistemology since Platon and Aristoteles. This is why Plautus originally more precisely phrased: One eye-witness is of more weight than ten hearsays. Those

who hear, speak of what they have heard; those who see, know beyond mistake. This is more or less the definition of the passion with which key opinion leaders as surgeon scientist driving the field of technical innovations forward. For me, personally, by the experience acquired in endoscopic enucleation of the prostate [2, 3], it was a small step to venture for ERBT in the shape of Tm:YAG laser en bloc mucosectomy for accurate staging of primary bladder cancer in 2010 [4]. To reach a sound base for the future one needs to look back. The first stocktaking of the already published studies set the agenda for the coming years [5]. It was puzzling from the start that a treatment with such great potential was not used sooner, had not taken off earlier. The march of ERBT started with a “sling polypectomy of bladder tumors” by Kitamura in 1980 [6] and as a circumferential incisive technique using current by Kawada [7] and using Holmium laser by Das and Gilling [8] in 1997. The spread of the technique came to a halt as did the proliferation for endoscopic enucleation of the prostate in the shape of HoLEP in the early 2000s [9].

With the advent of new lasers, namely, the continuous wave Thulium:YAG and Thulium fiber laser in 2005 [10, 11], that in the end led to a more conceptual way of

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Table 1 Exit strategies for tumor retrieval

	Author
Trapping and evacuation in extraction bags	Fritsche et al. [18]
Vaporization to reduce size of the specimen and extraction of the base only	Geavlete et al. [19]
Morcellation after securing the right resection level by “antegrade” resection	Sureka et al. [20]
Ellick evacuator or nephroscopy sheet and laparoscopic grasper for larger tumors	Hurle et al. [21]

Modified from Herrmann and Wolters [17]

understanding of surgical principles of anatomical enucleation of the prostate [3], a renaissance of reception of the “antique” en bloc resection technique of bladder tumors was about to start in 2011 [4]. Acteurs in the field of transurethral enucleation of the prostate, now familiar and embracing the concept of dissection along anatomical landmarks turned their focus on this technique. From the start of this renaissance the European Society for Uro-Technology (ESUT), with its chair Jens Rassweiler proved to be a sounding board for innovation. At the expert meeting of the ESUT and Section for Uro-Oncology (ESOU) on 2nd February, 2013 in Davos, Switzerland, ERBT data until 2013 were introduced to the uro-oncological peers [12]. ESUT could transfer a lot of enthusiasm in the meeting summary paper titling *Technical solutions to improve the management of non-muscle-invasive transitional cell carcinoma: summary of a European Association of Urology Section for Uro-Technology (ESUT) and Section for Uro-Oncology (ESOU) expert meeting and current and future perspectives* [13]. The results were certainly an imposition to the traditional TURB scene for two reasons: already having overseen the potential of early ERBT and probably having settled in an endoscopic therapy with known shortcomings and now being challenged. The beaming delta of lamina muscularis propria presentation (LMP) between ERBT and TURB of almost 25% coding for lower local recurrence and lower inter surgeon variance first need digesting [14]. The figures for LMP presentation in TURB specimens have just been reproduced by a current multicenter study with 71.1% in the TURB, and 80.7%, surprisingly low but still significantly better in the ERBT arm [15].

Maurizio Brausi as the author of EORTC studies [16] at that meeting wanted to send Udo Nagele and myself straight to Askaban when we topped the introduction of ERBT by suggesting vaporizing of the vast exophytic portion of the tumor and focus on the contact surface to the bladder wall. As good catholics Udo and I certainly deserve purgatory for something, but not for this push in solving the most urging inherent problem of the size limitation of specimen retrieval by sheath and in the end urethra. The “limitations” were clearly described at that time and approached ([17], Table 1).

The time was not right for this imposition by the power of two, although Bogdan Geavlete had tested this in a randomized controlled trial for TURB, published in 2012 [19]. It is good to see how the “overcoming the one piece extraction

dilemma” debate is moving on [22]. For myself, from the beginning, neither “one piece” nor “negative margins” were the direction but anatomical dissection and thereby accurate staging that would make the difference.

Udo Nagele and I also did not deserve purgatory for exploring endoscopic submucosal hydro-dissection (ESD), a technique from gastroenterology in ERBT and presented it in that same meeting. Adding of another modality, referred to as ERBT plus to distinguish from ERBT “only,” seemed to be feasible but not superior and brought another variability to the dissection plane by injecting saline [23, 24]. Unlike ERBT only in other studies, the Hybrid blue study, ESD finished with a LMP presentation of 86% in the ERBT arm, which might enlighten this fact [25].

Not only urologists headed in that direction, but also pathologists immediately were fond of ERBT and wanted the “TURBO,” as they concluded in 2013 that ERBT had the potential to overcome inherent problems of TURB specimen presenting cautery and crush artifacts as well as tangential rather than vertical sections allowing for spatial orientation in embedded tissue [26]. Furthermore, oncological principles known from other surgical fields seemed to be met in the principles that Ukai laid down 12 years before in 2000 with his publication of TransUrethral Resection of Bladder tumors in One piece (TURBO) [27].

ERBT coined as an acronym in 2014 would be general practice if [24] “Seeing is believing” would be true. The field of uro-oncological endoscopic surgery seems to be different and for good reasons asks for more evidence to arrive on the table of the debate than was available from 2011 till 2018. Reviewing the summaries of that time [17, 28–30] gaps were obvious. If it was not for the first larger multi-institutional publication of the experience of the EBRUC consortium (En Bloc Resection of Urothelial Cancer) formed by the ad hoc working group after the ESUT / ESOU meeting published in 2015 [31] proving what structured reviews before had produced. The key messages were as follows: The representation of the lamina muscularis propria in the pathology report was as high as 97.3% in all groups; excellent specimen quality; and low procedural associated morbidity, when compared to contemporary series of TURB covered in the EAU Guidelines on NMIBC, who introduced a dedicated section almost in textbook fashion on how to perform TURB in 2015 [32]. However, with growing evidence ERBT made

an entry into the EAU Guidelines on NMIB in 2017 [33], an important year not only for ERBT but also for myself deciding to leave Hanover Medical School and joining the Urological community in Switzerland (SGU). At this point I would like to sincerely thank Mario Kramer who was and still is a great collaborator not only because he largely composed our manuscripts, but he also aimed for the next level: a large multicenter randomized controlled trial. However, some gaps were closed in between by Rodolfo Hurlle and Lukas Lusuardi [34] when it came to technical aspects of the feasibility of TURB after ERBT. The international consensus in ERBT meeting in Hong Kong hosted by Jeremy Teoh [35] in 2020 defined the gap of knowledge, already tangible beforehand in earlier reviews and meta-analysis, to be filled.

After 2020, these high-quality randomized controlled trials arrived that were urged for in the past in the beginning of the renaissance. Almost all of my collaborators are displayed in the authors list of this special issue. I would like to personally thank those people that caught fire and marvelously conducted studies. All of them became passionate fellow campaigners not only for ERBT but also for improved training of residents and better surgery and outcomes for our patients: the study groups of Alberto Breda [36, 37], Jeremy Teoh [22], and Dimitry Enikeev [38] as well as the ESUT led by Ali Serdar Goezen [39] did a wonderful job for the delight of the reader and sake of the subject.

Jeremy Teoh who is the head of a global registry database [22] will deliver the evidence requirement of what we defined in the EUA guideline panel of Male LUTS as required certainty of evidence to implement ERBT as a first-line treatment option supported by the guidelines reaching the top of the evidence pyramid [48].

The efforts the urological community undertook in the last 15 years to get on top of uro-oncology and medical therapy of malignant disease are remarkable. However, even in 2023, I still sense at the same time disengagement of venturing for new surgical techniques. The problems of filter bubbles and echo chambers in knowledge societies are subjects [40, 41] of the contemporary version of the epistemology debate. These bubbles between endourology and uro-oncology do not seem to communicate well. A look in a different context is useful to enlighten this.

Platon would let Sokrates ask a person of the uro-oncology bubble in the fashion of hermeneutics, why the community was easily jumping for Abiraterone after data from

Cougar 301 study presented by Johann S de Bono et al. in [43] showing a difference in OS in mCRPC of 3.9 months (14.8 vs. 10.9 months) or embracing of Docetaxel after Ian Tannock presenting data of TAX 327 [44] study showing a difference of median survival of 2.4 months (18.9 vs. 16.5 months) and not immediately embracing ERBT by pointing the uro-oncology bubble member toward the “red” line in MIBC of 3 months. The EAU guidelines on muscular invasive bladder cancer (MIBC) refer to a meta-analysis including 19 studies concluding that a delay of > 3 months has a negative effect on OS. Although the authors highlighted the lack of standardization regarding the definition of delays, overall conclusion was that patients scheduled for radical cystectomy should be treated without delays to maximize survival [42].

However, every thought experiment lags behind but if you ask your colleague from the uro-pediatric surgeon bubble, who also will tell you about his appreciation of submucosal dissection for ureteral reimplantation, that it is a great deal to tackle problems right at the beginning to avoid further damage. A delay in definite treatment is potentially a lethal damage, and probably we can save a proportion of our patients from requiring (cost intensive) adjuvant treatment after definite treatment, when we do it right from the beginning. Can one believe that when f.e. Manni Mennon or Inderbir Gil had called for a surgical procedure with the robot that would have delivered an improvement of 25% in the pathological review of the surgical specimen in the 2000s, that the uro-oncological surgeons would have ignored that (like they did for ERBT)? I can hardly believe that. Be it cognitive bias or dissonance, or simply decision fatigue [45, 46]. We have to move on.

Concluding, on the footstep of the perron to the portal of a better staging and management of bladder cancer, where ERBT in my perception has arrived today, I want to approach the informed surgeon scientist with what large language models like ChatGPT already “know” about ERBT [47], and most probably all of your patients will most probably find out, supporting surgeons to venture for ERBT for various reasons (Table 2).

I hope that the readers of this Special Issue with the data of 2023 will enjoy reading it and that it will give them an impulse to actively turn to ERBT.

Table 2 What ChatGPT “knows” on ERBT [47]

Learning en bloc resection of bladder tumors can be important for several reasons

- Optimal tumor removal:** En bloc resection involves the complete removal of the tumor in one piece, minimizing the risk of leaving behind cancerous cells. This leads to a higher likelihood of complete tumor eradication, reducing the chances of recurrence
- Improved staging:** En bloc resection allows for a more accurate assessment of the tumor's size, depth of invasion, and involvement of adjacent structures. This information is crucial for determining the stage of bladder cancer, which guides treatment decisions
- Enhanced pathological examination:** When tumors are removed en bloc, they can be examined by pathologists more effectively. This aids in a precise diagnosis, helps determine the cancer's aggressiveness, and informs treatment planning
- Reduced risk of tumor spillage:** Traditional resection techniques can sometimes result in tumor fragmentation and the spread of cancer cells into the bladder or surrounding tissues. En bloc resection minimizes this risk, as the tumor is removed intact
- Better functional outcomes:** En bloc resection aims to spare healthy bladder tissue, preserving bladder function to a greater extent than more extensive surgeries like radical cystectomy. This can be particularly important for maintaining quality of life
- Less Risk of Perforation:** En bloc resection is performed with precision, reducing the risk of accidental bladder perforation compared to other techniques
- Potential for organ preservation:** For some early-stage bladder cancers, en bloc resection may be curative without the need for more aggressive treatments like cystectomy (removal of the entire bladder). This can be an important consideration for patients concerned about the impact of surgery on their daily life
- Minimized blood loss:** En bloc resection is often associated with less bleeding during surgery, which can lead to shorter hospital stays and faster recovery
- Treatment personalization:** Learning en bloc resection adds a valuable technique to a surgeon's repertoire. This enables them to choose the most appropriate surgical approach based on the patient's specific tumor characteristics and overall health
- Patient outcomes:** Studies have shown that en bloc resection can lead to better oncological outcomes and improved survival rates for certain bladder cancer patients
- In summary, learning en bloc resection of bladder tumors is essential for urologists and surgeons involved in the treatment of bladder cancer. It offers several advantages, including improved tumor removal, better staging, reduced risk of complications, and the potential for organ preservation, ultimately leading to better outcomes for patients

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