

# TULA in recurrent non-muscle invasive bladder cancer

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**Recent NICE guidance says there is limited evidence for the efficacy of transurethral laser ablation for recurrent non-muscle invasive bladder cancer and that 'special arrangements' need to be in place if it is to be offered to patients. Here the authors consider the advantages and drawbacks of the treatment.**

In July 2019, the NICE interventional procedures programme published its guidance on transurethral laser ablation (TULA) for recurrent non-muscle invasive bladder cancer (NMIBC) (see Box 1).<sup>1</sup> It is important to stress that, while it is often claimed (usually by the company marketing the device) that a procedure is 'recommended by NICE', this is not correct. The interventional procedures guidance does make 'recommendations' regarding the role of a procedure, but this is not the same as recommending a procedure (ie endorsing its use). Instead, the

programme's role is to consider if a procedure is safe and whether it would work well in the wider NHS. Bearing this latter point in mind, the actual 'recommendation' is that while the procedure may not be harmful to patients, its use and outcomes need to be carefully audited – which is obviously not the same as being 'recommended by NICE'. Furthermore, anyone can apply to the NICE interventional procedures programme, including the manufacturer of a medical or surgical device.

The current management of recurrent low risk (LR) NMIBC has remained largely unchanged for over 50 years, involving repeat general anaesthetic (GA) rigid cystoscopy and biopsies – often in frail patients without a life threatening condition. Given the increasing popularity of more conservative approaches in other cancers, such as high-intensity focused ultrasound in prostate cancer and radiofrequency ablation in kidney cancer, the NICE guidance on TULA serves as an opportunity to consider whether a more conservative approach to LR NMIBC would be more cost effective in the NHS.

However, TULA is not a new procedure and its clinical role has already been covered by the NICE bladder cancer guideline,<sup>2</sup> as well as the European Association of Urology (EAU) guideline on NMIBC.<sup>3</sup>

Interestingly, the NICE bladder cancer guidelines recommend fulguration (which is the same as laser ablation) without biopsy only in patients with a solitary recurrence and a tumour diameter of 3mm or less, while the EAU guidelines state that

'fulguration of small papillary recurrences on an outpatient basis could be a safe option'.

## The evidence

There are no randomised trials of TULA and the current evidence is based on level 3b/4 evidence (six case series and two non-randomised comparative studies – a total of 588 patients) with relatively short follow-up (median follow-up is one year). Local recurrence rates varied between 10–20% at 12 months, which compares well with a predicted 24% risk of recurrence at one year post surgery in this group of patients using the European Organisation for Research and Treatment of Cancer (EORTC) risk tables. Notably, all the studies reported high patient satisfaction, with rates of over 90%.<sup>4–6</sup>

## Advantages and drawbacks to TULA

Given the high level of patient satisfaction and acceptable recurrence rates, what are the other potential benefits of TULA? Because around 50% of new NMIBC tumours are LR NMIBC, it would be reasonable to treat small recurrences (<5mm) in this group of patients with TULA rather than subjecting them to an GA cystoscopy and biopsy. This would free up a significant number of GA cystoscopy slots in theatre that could be used for more timely treatment of higher risk NMIBC patients.

On the other hand, a major concern with TULA would be the lack of biopsy with a small risk of grade progression (to Grade 3) and stage progression (to T1 or T2); although, it is

### Box 1. Summary of NICE guidance for TULA<sup>1</sup>

- There are no major safety concerns
- Current evidence on efficacy is limited
- The procedure should only be used with arrangements for clinical governance, consent and audit in place
- Ensure that all patients understand uncertainties about the procedure's efficacy
- Audit clinical outcomes
- Patient selection should be done by a specialist bladder multidisciplinary team

reassuring that the EORTC risk tables suggest that risk of progression at one year in the LR NMIBC group is extremely low at 1%. A further concern is that a recent randomised trial of chemoablation in LR NMIBC (CALIBER) showed a surprisingly high biopsy-proven three-month recurrence rate (*ie* residual disease) in the surgical control arm of 20%,<sup>7</sup> many of who had ablation/fulguration rather than resection/excision, which raised concerns about incomplete destruction of a tumour with ablation compared to complete excision. In any case, the NICE bladder cancer guidelines recommend discharge of LR NMIBC patients who are recurrence-free after 12 months. If this practice was followed there would only be a narrow follow-up window (one year rather than five years) in which to apply TULA in this group of patients.

### Practical considerations for the use of TULA

Interestingly, the recommendations do not specify the type of laser that is to be used in TULA. Currently, the most commonly used laser is a holmium: YAG laser with a 6Hz laser frequency and 0.9kJ energy, reducing to 6Hz and 0.6kJ around the trigone and bladder neck area, which is more sensitive for patients.

One of the factors not covered by the NICE recommendations is the need for a very experienced flexible cystoscopist. In practice, it is often difficult to keep the laser fibre still for long in order to ablate a tumour, partly due to movement of the bladder wall with the patient's respiration. Also, some parts of the bladder are harder to reach with the laser fibre – most notably in the dome of a large-capacity bladder, and tumours in a heavily trabeculated bladder or diverticulae – with some tumours requiring the J manoeuvre to turn the cystoscope back on itself. Finally, a reasonable inflow of irrigation is required in order to keep the field of view clear, but as this fills the bladder up the patient

becomes progressively uncomfortable. These factors often limit the number of lesions, especially in a multifocal tumour, that can be treated by TULA (see Box 2).

Although many office urologists in Europe and the United States perform their own surveillance flexible cystoscopies and can have a laser on standby for every list, in the NHS only a proportion of flexible cystoscopy lists are likely to be performed by someone experienced in using TULA. In addition, the need for a laser-safe operating theatre, specialist laser operator and eye protection for all persons in theatre, means that TULA cannot immediately be used in the event of recurrence discovery during a surveillance flexible cystoscopy. In practice, patients usually must return to a dedicated TULA list, though this will still save a GA theatre case.

A further practical issue is that recurrent LR NMIBC patients suitable for TULA are also the group that are most likely to benefit from a single post-procedure instillation of mitomycin (EORTC recurrence score of <5, level of evidence 1a). Given the concerns around ablation leading to incomplete tumour destruction,<sup>7</sup> it therefore makes sense to include a single instillation of chemotherapy following TULA for maximum benefit. This, in turn, further limits the use of TULA to a dedicated flexible cystoscopy list manned by trained and experienced staff.

### Conclusion

The NICE interventional procedures guidance supports the use of TULA in the management of LR NMIBC.

In selected cases (and in the hands of an experienced flexible cystoscopist) TULA represents an attractive option for patients. However, it is important to note that LR NMIBC patients will usually still require treatment on a dedicated TULA list, and there are concerns about incomplete destruction of lesions using this technique.

### Box 2. Practical considerations for using TULA

- The procedure requires an experienced flexible cystoscopist
- It is often difficult to keep the laser fibre still due to the patient's respiration
- Irrigation is required to maintain a clear view, which can make the patient uncomfortable
- A dedicated laser-safe theatre, safety equipment and trained staff are also required
- In practice all these requirements mean a dedicated TULA list is required

**Declaration of interests:** none declared.

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