

Intravesical microwave hyperthermia with intravesical chemotherapy for superficial bladder cancer

1 Guidance

1.1 The current evidence on intravesical microwave hyperthermia with intravesical chemotherapy for superficial bladder cancer is based on small numbers of patients but raises no major safety concerns. The evidence on efficacy is very limited and treatment protocols have varied between the published studies. Therefore, this procedure should only be used in the context of controlled clinical research.

2 The procedure

2.1 Indications

- 2.1.1 Transitional cell carcinoma is the most common form of bladder cancer. It begins in the bladder lining (urothelium). Superficial disease is defined as cancer that is confined to the bladder lining and has not invaded the muscle layer.
- 2.1.2 Surgical interventions for superficial transitional cell carcinoma include transurethral resection (TUR), in which malignant tissue is removed with an electrocautery device during cystoscopy. Bacillus Calmette-Guérin (BCG) vaccine or chemotherapeutic drugs may be instilled directly into the bladder, either as a treatment in itself, or as adjuvant therapy after TUR. Cystectomy may be necessary in some patients.

2.2 Outline of the procedure

- 2.2.1 Intravesical microwave hyperthermia combined with intravesical chemotherapy can be used as neoadjuvant treatment prior to TUR to try to eradicate tumours. Alternatively, the procedure can be used as adjuvant treatment after TUR to try to prevent recurrence.

2.2.2 The procedure can be conducted on an outpatient basis using local anaesthetic urethral gel. A balloon catheter, containing an antenna and several insulated thermocouples, is inserted through the urethra into the bladder. Ultrasound is sometimes used to assess the position of the device. The antenna emits microwaves which heat the superficial layers of the bladder wall. The thermocouples, which are spread out from the catheter and pushed against the bladder lining, monitor temperature to help prevent overheating. A solution of cytostatic agent, usually mitomycin C, is instilled into the bladder, between the bladder wall and the balloon surface. The solution is continuously pumped out of the bladder, cooled, and recirculated to prevent overheating. Treatment sessions usually last for 40–60 minutes and are usually repeated weekly for 4–8 weeks, or longer for adjuvant treatment.

2.3 Efficacy

- 2.3.1 Studies of the procedure as neoadjuvant treatment before TUR assessed response to treatment by histology, cytology or cystoscopy. One randomised controlled trial (RCT) and one non-randomised trial reported that a complete response was more frequent with combined hyperthermia and mitomycin C treatment than with mitomycin C alone (RCT: 66% [19/29] vs 22% [5/23], $p < 0.001$; non-randomised trial: 66% [19/29] vs 28% [10/36], p value not reported). Two case series reported a complete response in 70% (31/44) and 75% (21/28) of patients.
- 2.3.2 In the RCT, tumours recurred more frequently in patients treated with mitomycin C alone (39% [9/23], mean follow-up 36 months) than those

Interventional procedure guidance 235

This guidance represents the view of the Institute, which was arrived at after careful consideration of the available evidence. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. This guidance does not, however, override the individual responsibility of healthcare professionals to make appropriate decisions in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer. Interventional procedures guidance is for healthcare professionals and people using the NHS in England, Wales, Scotland and Northern Ireland.

This guidance is endorsed by NHS QIS for implementation by NHSScotland.

treated with combined treatment (28% [8/29], mean follow-up 38 months, difference not significant). One case series of 44 patients reported that 18% of patients (7/38) with recurrent disease before the procedure had tumour recurrences. A case series of patients with grade G3 tumours at baseline reported that 21% (6/28) of patients were referred for cystectomy during follow-up (median 15 months).

2.3.3 Using the procedure as adjuvant treatment following TUR, an RCT reported that tumour recurrence during 24-month follow-up was significantly more frequent in patients treated with mitomycin C alone (56% [23/41]) than in those treated with combined treatment adjuvant to TUR (14% [6/42], $p = 0.0002$). A case series of 90 patients reported risk of tumour recurrence as 14.3% (standard error [SE] 4.5%) and 24.6% (SE 5.9%) after 1 and 2 years respectively. In another case series of 24 patients with grade G3 disease, 38% (9/24) experienced tumour recurrence, on average 10 months after the first treatment session. For more details, refer to the 'Sources of evidence' section.

2.3.4 The Specialist Advisers considered this procedure to be of uncertain efficacy. One Specialist Adviser commented that the long-term effects of the procedure have not been evaluated, and nor has its suitability for all types of patients. One Specialist Adviser thought that the potential for tumour recurrence is the key efficacy outcome for the procedure.

2.4 Safety

2.4.1 In one RCT, 7% of patients (3/42) receiving adjuvant treatment developed urethral stricture compared with 2% (1/41) of those receiving mitomycin C alone (difference not significant). Urethral stricture occurred in 2% (1/44) and 4% (1/28) of patients in two case series of neoadjuvant treatment, and in 4% (4/90) of patients in a case series of adjuvant treatment.

2.4.2 Skin rashes in response to mitomycin C were reported in 2% (1/44) to 7% (2/28) of patients treated with combined neoadjuvant treatment and in 8% (2/24) to 12% (5/42) of patients treated with combined adjuvant treatment. In the latter study, 5% (2/41) of patients treated with mitomycin C alone also experienced skin rash (difference not significant).

2.4.3 Most patients across the studies reported symptoms of cystitis for 1–2 days after each treatment session. Using a symptoms questionnaire (minimum score 7, maximum 24), one RCT of neoadjuvant treatment reported that the mean score was 18.3 (standard deviation [SD] 2.3) in the combined treatment group and 13.1 (SD 2.1) in the mitomycin C-alone group, after 4 of the 6–8 treatment sessions (p value not reported).

2.4.4 In the RCT of adjuvant treatment, pain during treatment was reported by 40% of patients (17/42) in the combined treatment group compared to none in the mitomycin C-alone group ($p < 0.001$). A case series of 28 patients, treated with neoadjuvant treatment, reported pain during treatment in 6 patients (21%), dysuria lasting longer than 48 hours in 16 (57%), bladder spasms in 4 (14%) and urinary tract infection in 2 (7%). For more details, refer to the 'Sources of evidence' section.

2.4.5 The Specialist Advisers stated that theoretical adverse events include symptoms of severe cystitis such as dysuria, haematuria and bladder pain, tissue reaction, thermal injury to the bladder (usually minor and transient), skin reactions, bladder contracture, extravasation and chemical peritonitis.

Andrew Dillon
Chief Executive
October 2007

Information for patients

NICE has produced information describing its guidance on this procedure for patients and their carers ('Understanding NICE guidance'). It explains the nature of the procedure and the decision made, and has been written with patient consent in mind. This information is available from www.nice.org.uk/IPG235publicinfo

Sources of evidence

The evidence considered by the Interventional Procedures Advisory Committee is described in the following document. 'Interventional procedure overview of intravesical microwave hyperthermia with intravesical chemotherapy for superficial bladder cancer', March 2007.

Available from: www.nice.org.uk/ip395overview

Ordering information

Copies of this guidance can be obtained from the NHS Response Line by telephoning 0870 1555 455 and quoting reference number N1350. 'Understanding NICE guidance' can be obtained by quoting reference number N1351.

The distribution list for this guidance is available at www.nice.org.uk/IPG235distributionlist

Interventional procedures guidance makes recommendations on the safety and efficacy of a procedure. The guidance does not cover whether or not the NHS should fund a procedure. Decisions about funding are taken by local NHS bodies (primary care trusts and hospital trusts) after considering the clinical effectiveness of the procedure and whether it represents value for money for the NHS.

© National Institute for Health and Clinical Excellence, 2007. All rights reserved. This material may be freely reproduced for educational and not-for-profit purposes. No reproduction by or for commercial organisations, or for commercial purposes, is allowed without the express written permission of the Institute.