

# ENDOSCOPIC MACROPLASTIQUE™ INJECTION FOR THE TREATMENT OF FEMALE STRESS INCONTINENCE: ROLE AND EFFICACY

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## ABSTRACT

This study was carried out to evaluate the role, safety and efficacy of endoscopic Macroplastique™ implants in the management of female stress incontinence. Between 1995 and 1999, transurethral submucosal injection of Macroplastique™ was performed in 68 women (mean age 58 years, range 32-85 years) for the treatment of genuine stress incontinence. Fourteen patients had undergone previous surgery for incontinence that had failed to correct the problem. Under general or regional anaesthesia, the Macroplastique was injected submucosally 1 cm distal to the bladder neck at 3, 6 and 9 o'clock positions. In 26 cases the 12 o'clock position was chosen to ensure a good occlusion of the bladder neck. The mean volume of Macroplastique injected was 3 ml. At a mean follow up of 19 months, 24 patients (35.3%) were dry, 18 patients (26.5%) were improved and 26 patients (38.2%) were still wet. Complications were all minor. We conclude that transurethral submucosal injection of Macroplastique™ should be used in women with mild to moderate stress incontinence who have failed to respond to physiotherapy. Being a minimally invasive day case procedure with low morbidity which can be repeated if necessary and has a satisfactory success rate, we believe Macroplastique implantation could be a good alternative line of treatment for stress incontinence.

## INTRODUCTION

Urinary incontinence is a common but often neglected condition. The prevalence of urinary incontinence increases with age; 10 to 25% of women under age 60<sup>1</sup> and more than 50% of nursing home residents are affected by this condition<sup>2</sup>. Genuine stress incontinence is a major contributor to urinary incontinence with an estimated prevalence of 21 to 46%<sup>3,4</sup>.

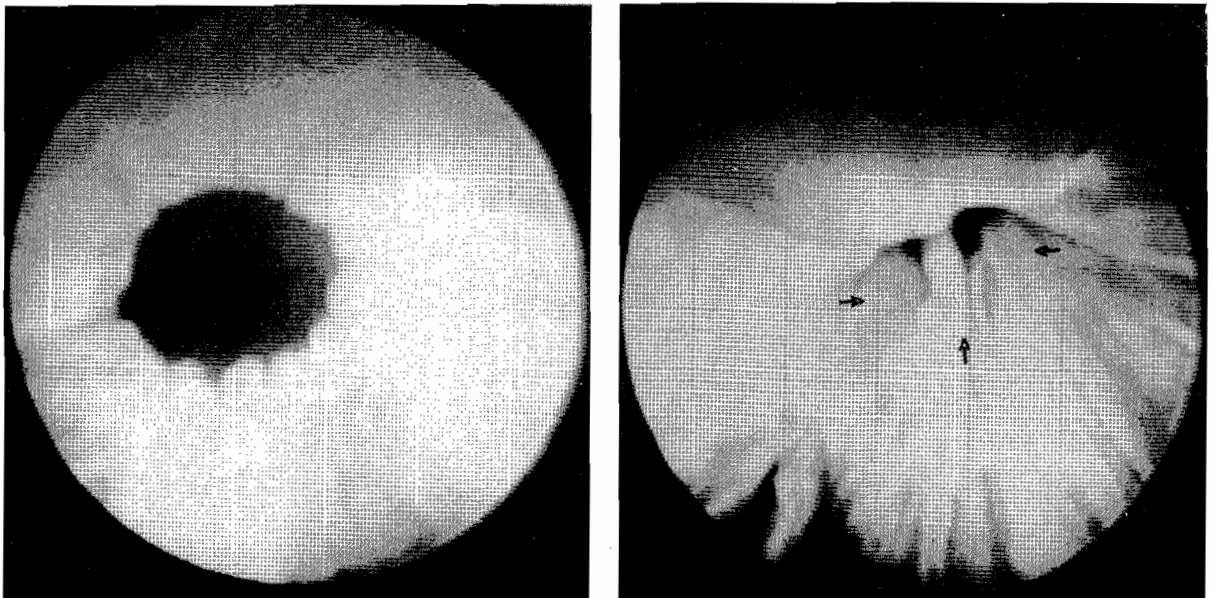
The idea of bulking the periurethral tissue to relieve female urinary incontinence is not new. Various procedures to correct stress in-

tinence by periurethral injections of substances that compress, support or narrow the bladder neck have been designed<sup>5</sup>. The major problems associated with the early agents included local tissue damage and the development of both clinical and radiological pulmonary emboli<sup>6</sup>. Recently, several different centers have published extremely encouraging results with Macroplastique for endoscopic treatment of stress incontinence<sup>1,6,7</sup>.

In this study, we report our results and evaluate the role, safety and efficacy of this procedure.

**Table 1:** Previous Surgery for Incontinence, Hysterectomy or Combined

Previous Surgery	No. of Patients
Pubovaginal rectus fascial sling	1
Burch Colposuspension	3
Hysterectomy	19
Hysterectomy & Marshall-Marchetti-Krantz Cystourethropexy	10
No previous surgery	35
<b>Total</b>	<b>68</b>



**Fig. 1:** A: Bladder neck before injection. B: Bladder neck after injection. Arrows show occlusive urethral mucosal blebs at three points (3, 6 and 9 o' clock)

**PATIENTS AND METHODS**

Between 1995 and 1999, 68 females suffering from stress incontinence were treated with transurethral submucosal injections of Macroplastique™. Their age ranged from 32 to 85 years (mean age 58 years). Fourteen patients had undergone previous surgery for incontinence that had failed to correct the problem. Ten of them had had combined continence surgery and previous hysterectomy while previous hysterectomy alone was reported in

19 patients (Table 1). All hysterectomies were done for non-malignant causes.

Preoperative assessment included a careful history, urogynaecological examination, pad weighing (only when stress incontinence could not be detected clinically), video-urodynamics and Valsalva leak point determinations.

The post-void residual bladder volume was measured ultrasonographically before surgery. Patients who could not empty their bladders

**Table 2:** Results of Macroplastique Injection in 68 Patients

Previous Surgery	No. of Patients	Cure	Improvement	Failure
Previous continence surgery	4	1	2	1
Hysterectomy	19	9	5	5
Hysterectomy & Continence surgery	10	3	3	4
No previous surgery	35	11	8	16
<b>Total</b>	<b>68</b>	<b>24</b>	<b>18</b>	<b>26</b>

well before surgery were excluded from the study as they were likely to have marked voiding problems afterwards.

In our study, only patients with mild to moderate stress incontinence who had failed to respond to physiotherapy, patients unfit to undergo a more invasive procedure or who refused open surgery were included. None of our patients had a significant vesical descent. Patients with detrusor instability were excluded.

Under general or regional anaesthesia, an area nearly 1 cm just distal to the bladder neck was visualized endoscopically. A special straight pre-lubricated needle was used. A small amount of Macroplastique implant was expressed at the tip of the needle before perforating the mucosa of the urethra; the Macroplastique paste was then injected submucosally by a special high-pressure administration gun with the objective of achieving a narrowing of the urethra towards the bladder neck. The needle should be kept well beneath the mucosa to avoid the formation of thin blebs or blisters, which may rupture and cause loss of paste. The 3, 6 and 9 o'clock positions were used in all our cases (Fig 1), while the 12 o'clock position was sometimes chosen to ensure a good occlusion of the bladder neck (26 cases). The mean volume of Macroplastique injected was 3 ml. Continence with a full bladder was confirmed at the end of the procedure by abdominal pressure. Antibiotics were routinely given post-operatively. Urethral catheterization was not a routine after injection.

## RESULTS

The follow up ranged from 3 to 32 months (mean 19 months). The patients were as-

sessed and the results were analyzed and divided into three categories: cure, improvement and failure. The patient was considered as cured when she was dry, fully continent and wearing no protection by the end of the follow-up period, while improvement was defined as a satisfactory reduction in the degree of stress incontinence without achievement of total dryness. Improved patients experienced only minimal leakage, but still required changing underwear or wearing protection; all our improved patients were personally satisfied with the results of the operation. Failure was considered when the patient had remained incontinent without any significant improvement post-operatively or by the end of the follow up period.

Most of our patients required a single injection. Only 5 patients were subjected to a second injection 4 to 7 months later. Four of them became dry, while one patient noted no improvement.

At a mean follow up of 19 months, 24 patients (35.3%) were dry, 18 patients (26.5%) were improved, with an overall improvement of 61.8% (Table 2).

Further surgical interference was needed in 26 patients (38.2%) who were still wet (failure). Of these 26 failures, 6 patients were dry at a mean postoperative follow up of 3 months, but failure was the end result after a mean follow-up of 7 months. Five of them were asthmatic.

Complications were all minor. Mild urethral burning and local discomfort were common in the early postoperative period and were successfully managed by non-steroidal anti-inflammatory treatment. None of our patients had urinary tract infection post-operatively. One

patient had fever due to bronchitis. Temporary urinary retention was observed in 4 patients (5.9%), which required urethral catheterization for few days (24 – 72 hours).

## DISCUSSION

Urinary incontinence is a distressing and demoralizing condition that affects 10-25% of women between the age of 15 and 60 years<sup>1</sup>. One common type of urinary incontinence is stress urinary incontinence. Genuine stress incontinence is a major contributor to urinary incontinence with an estimated prevalence of 21-46%<sup>3,4</sup>.

Normal continence in female patients results from the musculofascial components maintaining normal anatomical support and position of the bladder, along with an intrinsically intact urethra with its coapting mucosal surface. Failure of one of the components will not necessarily produce stress incontinence, if the other components are intact<sup>8</sup>.

Patients with simple stress incontinence should be distinguished from those who have an unstable bladder. The management of each is different, and those patients with a combined picture of bladder instability and stress incontinence benefit from treatment of the instability in first place.

Since the first description of a procedure for the treatment of continence, more than 150 techniques and modifications have been proposed for the management of stress urinary incontinence<sup>9</sup>. Intrinsic urethral sphincter deficiency can be managed by many techniques. Such patients require procedures that produce urethral compression or coaptation by the use of slings, artificial urinary sphincters or transurethral injections<sup>1</sup>. Suspension procedures are designed to restore the anatomy of the bladder neck and the proximal urethra by elevation to their normal resting position<sup>9</sup>.

Periurethral injectables seem to be a reasonable option in the modern treatment of female urinary incontinence<sup>5</sup>. However the actual mechanism of implantation therapy is unknown and is probably multifactorial with some obstructive component<sup>6</sup>. Eckford and Abrams<sup>10</sup> reported that obstruction of the bladder neck by periurethral injections which augment urethral mucosa and improve coaptation and intrinsic sphincter function is the mechanism by which

continence is achieved. Later reports by Monga and Stanton<sup>11</sup> and Khullar et al.<sup>12</sup> suggested that obstruction was not the mechanism by which periurethral injections produce continence. In successfully treated patients, the results of periurethral injections is the cephalad elongation of the urethra with a concomitant increase in the pressure transmission ratio in the first quarter of the urethral length. These changes result from the placement of the injectables at the bladder neck or proximal urethra, which, when properly positioned, can prevent bladder neck opening under stress. A more distal deposition of the injectable will not increase the functional urethral length or prevent the bladder neck opening during episodes of increased intraabdominal pressure.

However, it still remains controversial which material to use. An ideal substance should incur no risk to the patient, be simple to use, allow easy repetition in the event of failure, be financially competitive and should not diminish the future treatment options<sup>6</sup>. The treatment of female urinary incontinence by periurethral injectable materials was originally reported by Murless in 1938<sup>13</sup>, but only became popular with the use of Polytef<sup>14</sup>. Unfortunately, the use of Teflon has several potential disadvantages. Severe local scarring from the injection makes subsequent continence surgery difficult, if not impossible. In addition, concerns have been expressed about its safety; granuloma formation<sup>15</sup> and the distal migration<sup>16</sup> of Teflon particles to the lymph nodes, lung and brain have been well documented in experimental<sup>17</sup> and clinical studies<sup>18,19</sup>. Also, it has satisfactory short-term results, but long-term success rates seem to decrease<sup>20</sup>.

In the late 1980s, a certain composition of bioactive glasses known as Bioglass (calcium oxide) was identified at the University of Florida that could elicit favourable responses in the host. However, this material has not yet been tested in humans<sup>21</sup>.

The interest in periurethral injectables resulted in the use of collagen and autologous fat as periurethral bulking compounds. They eliminate the risks of local and distant foreign-body reactions. These materials are, however, absorbed very rapidly, so that more than one injection is often necessary and there is a time-dependent decline in their efficacy<sup>22</sup>. Also, collagen being a foreign protein, it elicits a cell-mediated and humoral immune response. Therefore, skin testing is essential to exclude

patients with a pre-existing hypersensitivity to bovine collagen (2-3%)<sup>9</sup>.

Macroplastique™ consists of sterile, non-pyrogenic, solid-textured polydimethylsiloxane (silicone rubber) particles suspended in a non-silicone carrier gel. The silicone particles are encapsulated in fibrin and act as a bulking agent while the non-silicone carrier gel is absorbed by the reticuloendothelial system and excreted unchanged (not metabolised) from the body through the kidneys. Most of the particles (75-99%) are in the range of 100 to 450 µm in diameter<sup>5</sup>. Because they are large, the silicone particles cannot be phagocytosed by macrophages, making migration unlikely. The fibrous capsule remains stable after formation and this is considered to prevent any further escape or migration at a later stage. Therefore, a permanent or longer lasting result should be expected<sup>9</sup>.

We have been using Macroplastique for over five years. We perform the procedure as a day case, and it only takes an average of 15 minutes to complete. We have found that, while there is a learning curve, once one learns to perform the procedure correctly, it is unnecessary to use large amounts of the material to achieve good results. Macroplastique is not very expensive, especially when compared to the cost of hospitalization after an operation.

As with any other procedure, one of the factors affecting success rate is patient selection. According to Koelbl et al., a patient presenting with poor urethral function, lack of detrusor instability and a good anatomic support is considered an ideal candidate for transurethral injections<sup>1</sup>.

The use of Macroplastique does not appear to prejudice open surgery at a later date if the incontinence persists. Furthermore, the injection appears to be equally effective in women who underwent previous incontinence surgery<sup>7</sup>. This is also in accordance with Benshushan et al. who stated that the periurethral injection was likely to be a useful adjunct to other operations, particularly in those cases where the bladder neck had been adequately resuspended, but leakage persisted due to a continuing problem with poor urethral function<sup>5</sup>.

After a mean follow up of 19 months, 35.3% of our patients were dry, and 26.5% were improved, with an overall improvement of

61.8%. Further surgical interference was required in 38.2% of our patients who were still wet (failure). Most of our patients only required a single injection. Although the mean volume of Macroplastique injected (3 ml) was less than that used in other studies<sup>6,7</sup>, our results were comparable to their results. Harriss et al.<sup>7</sup> reported that, after 3 years, 40% of their patients had remained completely dry, 18% had improved and 42% required alternative treatment, while Sheriff et al.<sup>6</sup> reported an overall success rate of 48% at 2 years of follow up. According to Khullar et al.<sup>12</sup>, the quantity of the injectable is not related to cure, which also suggests that the placement of the injectable is more important than the bulk effect of the injectable itself<sup>6</sup>.

Sheriff et al.<sup>6</sup> reported that the reason for the drop in the success rate after the first and third months is not entirely clear, although it may partly be due to the reduction in coaptation of the bladder neck consequent upon the maturation of the inflammatory reaction following the injection of the material and absorption of the carrier medium. Loss of the material through the injection site may also occur as early as on the first postoperative day.

Patients often have a "mixed picture" of both stress and urge incontinence. The Macroplastique will treat stress incontinence successfully and the patients will no longer leak when coughing or laughing; however, as the urge incontinence goes untreated, they may still be wet. This creates a large group of patients with intermediate or "improved" results who, in fact, no longer have stress incontinence but are still wet due to urge incontinence.

Transurethral injection of Macroplastique should be used in patients with mild to moderate stress incontinence who have failed to respond to physiotherapy. Also, being a minimally invasive procedure with a low morbidity that can be repeated if necessary, it is suitable for women who are at high operative risk as well as those with previously failed surgery. We believe that Macroplastique implantation could be a good alternative line of treatment for stress incontinence.

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