

Title: Long- term Safety and Efficacy of Polydimethylsiloxane (Macroplastique®) in Female Patients with Stress Urinary Incontinence: Analysis of Patients Who Completed 3- Years of Treatment.

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Introduction: Macroplastique (MPQ) is a urethral bulking agent (UBA) used in the treatment of stress urinary incontinence (SUI) in women with intrinsic sphincter deficiency (ISD). UBA of various materials have been studied as early as the 1930s. MPQ has been shown to have a good safety profile with no carcinogenic effects. It is constructed of a silicone elastomer with a large diameter of 140 µm suspended in a lower molecular weight gel. The elastomer has a rough configuration that interlock. These are unique properties of the material that do not allow for migration once implanted under the mucosa of the urethra [1]. The durability of MPQ has been shown in patients who were successful at one year and followed up to 2 years in a previous study. They maintained high success rate and demonstrated up to a 67% dry rate but even higher improvement rates of incontinence in the short term, 75% [1, 2]. The purpose of this study is to evaluate the safety and efficacy of MPQ in women with SUI due to ISD who completed 3-year follow-up in this post market study.

Methods and Materials: This is a retrospective review of prospectively collected data of 276 subjects enrolled in a multicenter study between October 2008-August 2017. A total of 21 centers in the United States were enrolled. Institutional review board approval along with patient informed consent were obtained for this study. Inclusion criteria were female at least 18 years of age, diagnosed with stress urinary incontinence due to intrinsic sphincter deficiency, subject understanding of all the study material including the five-year follow up schedule, and psychologically stable subject who would be suitable for the intervention as determined by the investigator. Subjects were excluded if they had an acute urinary tract infection/inflammation, pregnant or intended pregnancy within one year, had a sling placement within 12 weeks, had a bulking agent within 12 weeks, bladder neck, urethral stricture, vaginal prolapse, untreated detrusor instability/overactivity, neuropathic bladder, or overflow incontinence.

A total of 70 subjects completed a 3-year follow up. Subjects were treated with up to two MPQ injections and followed at 3,12, 24, and 36 months. Outcome was measured by change of Stamey grade (0= continent, 1= incontinence with vigorous activity, 2= incontinence with minimal activity and 3= total incontinence) and quality of life questionnaire (I-QoL) [3]. I-QoL divided into 3 subscales (Avoidance & Limiting Behavior, Psychosocial Impacts, Social Embarrassment) were assessed at baseline, 12, 24,and 36 months post injection. Patient Global Impression of Satisfaction (PGI-S) was then assessed at 36 months. The primary outcome of this study is to assess the success as measured by improvement to Stamey grade 0 or 1 at 36 months. Safety assessment is reported as serious and non-serious adverse events (AE). Two-sided binomial test

was used to test the overall success rate, while linear mixed effect model with patient-level random effect was used to examine longitudinal trends over the 3-year study period.

Results: The majority of patients were white, 67/70 (96%), with mean age of 63.3 years. 24/70 (34%) subjects underwent two injections. At 36 months, 21/70 (30%) of patients reported Stamey grade 0 and 28/70 (40%) had Stamey grade 1. The overall satisfaction was 68% at 36 months. 27/70 (38.5%) patients report they were very satisfied on PGI-S at 36 months. I-QoL scores and the subscales were significantly improved at 12, 24 and 36 months from baseline ($p < 0.0001$) and remained stable (Figure 1). The composite success rate (I-QoL, PGI-S and Stamey grade improvement) was 51.4%. Transient dysuria 3.2%, hematuria 6%, pain at the injection site 1.6% and urinary tract infection 2% were the most common non-serious AE that occurred within the first 3 months post injection. No serious AE were reported in these 3 years.

Interpretation of Results:

Composite outcome was determined by combining the subject reported outcomes based on the questionnaires and some degree of objective improvement as based on Stamey grade. Using a standardized questionnaire allows for longitudinal follow up that has shown the sustainability of satisfaction over the years even if some subjects required repeat injection. Subjects may have improved within their own Stamey grade therefore accounting for a higher overall satisfaction when compared to the composite success rate. One could argue that measures such as pad weight or urodynamic testing could be used to evaluate the success of UBAs, validated questionnaires such as the I-QoL and PGI-S are sufficient to evaluate subjective outcomes. This subjective improvement is significant when it comes to treating conditions that effect quality of life such as SUI.

The injection is also safe seeing that non-serious AE resolved in a short period of time and no patient deaths or serious AE occurred in this cohort. A recent publication demonstrated that surgeon skill level and pelvic radiation history was correlated with failure of MPQ [3]. While the surgeon experience was not captured in this study, the ease of administration of the implant by a minimally invasive, endoscopic route can account for the low risk and assuring complication profile in this study.

Concluding Message: At 3 years, MPQ is safe and efficacious for the treatment of SUI secondary to ISD in women. The overall a high satisfaction rate is sustained from baseline to 3 years post injection. Most complications are minor and transient in nature without sequelae.

[1]

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3. Serati M, Soligo M, Braga A, Cantaluppi S, Coluccia AC, Di Dedda MC, Salvatore S, Cetin I, Ghezzi F, Publication Committee of the Italian Society of U: **Efficacy and safety of polydimethylsiloxane injection (Macroplastique(R)) for the treatment of female stress urinary incontinence: results of a series of 85 patients with >/=3 years of follow-up.** *BJU Int* 2019, **123**(2):353-359.

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