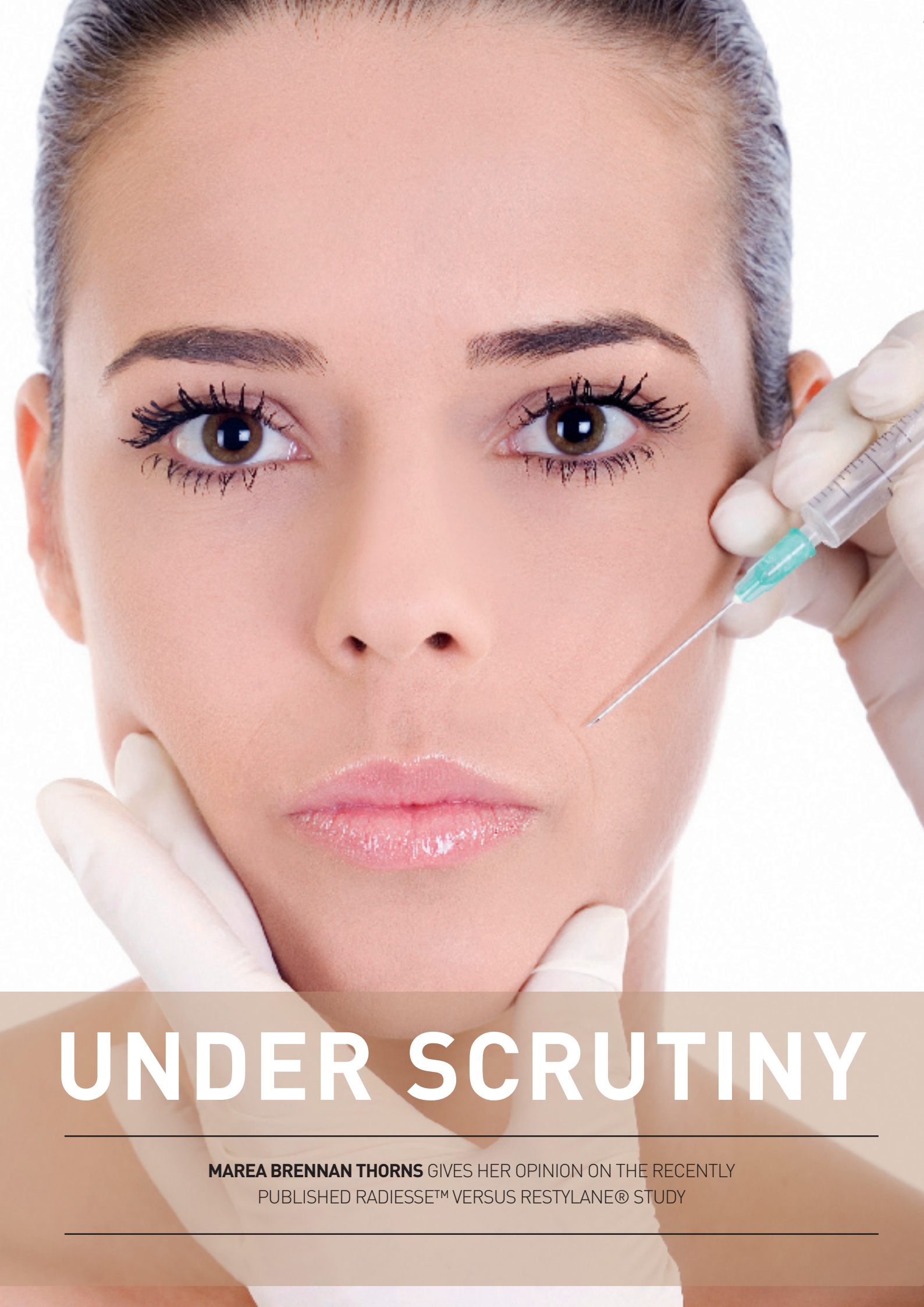

UNDER SCRUTINY

MAREA BRENNAN THORNS GIVES HER OPINION ON THE RECENTLY PUBLISHED RADIESSE™ VERSUS RESTYLANE® STUDY

As an advanced nurse practitioner, I regularly assess published research according to its relevance to my work and practice. The Critical Appraisal Skills Programme (CASP) tool (Enock et al, 1998), suggests we look at the following broad areas when appraising clinical studies:

Are the results of the study valid?
What are the results?
Will the results help me and my patient population?

It was therefore with interest that I read the brief summary of the findings of Moers-Carpi and Tufet (2008) in the February issue of *Aesthetic Medicine*. Although the results of the study appear valid in the first instance, comparing the duration of effect of a semi-permanent agent with that of a non-permanent agent seems questionable. The authors highlight the longer duration of effect of the calcium hydroxylapatite filler (CaHa; Radiesse™) when compared to the resorbable hyaluronic acid filler (NASHA™; Restylane®) when by their very classification they will have a different period of efficacy.

The exact period of time that CaHa remains in the body is not really known but Mayer et al (2001) speculate that it may last for up to seven years. Whilst this may be an attractive proposition to some patients initially, the extended duration of CaHa in the body raises an important safety issue. Currently, there is no available mechanism by which it can be dissolved if there is dissatisfaction with the treatment outcome or an adverse reaction. Although CaHa is biocompatible, it is not without adverse effects (Jansen et al, 2006) and there is a lack of long-term safety data concerning its use. In comparison, NASHA™ gels have been used in over seven million treatments with an extremely low rate of transient adverse events (0.06-0.15 per cent) (Friedman et al, 2002).

The authors compared the efficacy and duration of CaHa with a NASHA™ gel (Restylane®) more suited to the correction of moderate lines and wrinkles, for example, the oral commissures and glabellar lines. A more valid comparison is with the NASHA™ gel, Perlane®, which is more suitable for injection into the deep layer of the dermis and/or the surface layer of the subcutis in the correction of nasolabial folds. Study validity would also have been enhanced if the NASHA™ gel had been injected using the correct gauge needle (the IFU specifies a 30 G needle). The timing of the top-up (at four months) and follow-up at eight months also deviate from the product's IFU.

My second point relates to opportunity for bias within the clinical study. Although a blinded, randomised study, it involves a split face comparison which does not allow for the natural asymmetry that often exists in presenting patients. In addition, injection technique (for example, use of anaesthetic) and full correction was left to the discretion of the treating physician.

It is worth noting that a comparison between CaHa and Perlane® has already been reported (Moers-Carpi et al, 2007) and, as with the study under discussion here, the validity of the results can be questioned. The authors compared a semi-permanent (CaHa) and non-permanent agent (Perlane®); there was deviation from the Perlane® IFU with regard to top-up and follow-up and there were opportunities for bias in the study protocol.

The authors' findings on NASHA™'s duration of effect do not reflect previous published reports when compared with other non-permanent fillers. Carruthers et al (2005) compared the efficacy of Restylane Perlane® with that of a hylan B gel (Hylaform®) in the treatment of moderate to severe nasolabial folds in 150 patients. At six months post-treatment, a higher proportion of patients showed a 1-grade improvement in Wrinkle Severity Rating Scale (WSRS) score with Restylane Perlane® (75%) than Hylaform® (38%). Restylane Perlane® was considered superior in 64% of patients compared to only eight percent superiority in Hylaform® patients.

Lindquist et al (2005) compared Restylane Perlane® with a bovine collagen preparation (Zyplast®) in the treatment of prominent nasolabial folds in 68 patients. Investigator-based and patient-based ratings (Global Aesthetic Improvement Scale [GAIS] and WSRS) both indicated that Perlane® was significantly more effective than Zyplast® in maintaining cosmetic correction at nine months. Perlane® was superior to Zyplast® at six and nine months after baseline in 50.0% and 48.8% of patients respectively according to the WSRS. According to the investigator-based GAIS, Perlane® was superior to Zyplast® in 48.8% of patients nine months post-baseline compared to only 14.0% superiority with Zyplast®.

More recently, Narins et al (in press) presented data at the American Society of Dermatologic Surgery on the 18-month efficacy of a two-injection treatment regimen using NASHA™ gel. The study demonstrated that 97% of patients had at least a 1-grade improvement at 18 months and many had a 2-grade improvement according to the GAIS and WSRS. The 18-month improvement over baseline seen with this treatment regimen reflects the findings of Wang et al (2007), that the effect of NASHA™ is amplified by injection-stimulated collagen production and collagen breakdown inhibition that outlasts the filling of space by the injected gel.

When considering how these results will help my work with patients, I feel that any cost advantages of CaHa are minimal, as use of any remaining product in other areas of the face is limited due to the potential for adverse effects, particularly in the lip area (Jansen et al, 2006). Secondly, being unable to rectify over-correction is an important consideration. It limits product use to highly-experienced practitioners and minimises the number of patients who can potentially benefit. However, with a biodegradable product such as NASHA™, all practitioners can achieve a similar long-term effect to that achieved with permanent material whilst offering patients a better safety profile.

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