ULTHERA UPDATE WHITE PAPER:

Introduction of the 1.5mm Shallow Transducer

INTRODUCTION OF THE 1.5 MM TRANSDUCER

The Ulthera System is currently marketed world-wide and was approved by the FDA in 2009 for use as a non-invasive dermatological aesthetic treatment to lift the brow. Ulthera Inc. has offered a choice of three transducers to target either the deep dermis (3 mm) or the superficial muscular aponeurotic system (SMAS) layers (4.5 mm). These transducers have been clinically proven to provide a significant tightening and a lift to the brow for those seeking facial rejuvenation [1]. However, in an effort to provide a more complete multi-dimensional lift and dermal rejuvenation, Ulthera is now offering a 1.5 mm (10 MHz at 0.25 J) shallow transducer which has been used recently in clinical trials, a limited pre-release in the US and outside the US, and was available commercially to all US customers in February 2012. As with all energy-emitting devices that target the more superficial dermis, there may be concerns as to whether adverse events will occur when energy is placed more superficially with the new 1.5mm transducer. This is especially true for patients with Fitzpatrick skin types IV-VI who may be at higher risk for dyspigmentation and/or keloid formation following more superficially targeted treatments. However, the Ultherapy System bypasses the outer layers of the dermis to target the tissues at a specific depth. This differentiates the Ulthera shallow 1.5 mm treatment from that of other energy-based devices that serve to treat the same depth. Data from clinical trials and pre-release use are described below.

LIMITED PRE-RELEASE AND CLINICAL TRIAL FINDINGS

A limited number of physicians were provided with the 1.5mm transducer for clinical use in the areas they thought were most appropriate for this transducer which targets a more superficial depth, or per study protocol if conducting an Ulthera-sponsored study. Table 1 below lists the numbers of patients treated, the treatment density (number of lines delivered), and any reported adverse events.

As evidence by the pre-release use, the 1.5mm transducer has been used safely on the face and neck, and has been used as part of a full-face and neck treatment in combination with the transducers targeting 3.0mm and 4.5mm.

We feel this preliminary record of safety justifies the release of the transducer, along with treatment guidelines based on initial physician use (Table 1). However, the importance of proper technique should be stressed to all healthcare professionals who wish to use the 1.5 mm transducer. As with the other transducers, special care should be taken to ensure transducer contact is optimized so as to avoid possible adverse events as technique can be a more critical component when dealing with the shallower tissue planes. Adverse event reports will be monitored closely to ensure that there is no increase in events related to use of this transducer. If there is an increase in events, treatment guidelines will be revisited in order to address any safety risk. To this point, all effects observed to date, either probably or possibly related, have resolved **(see Table 1)**.

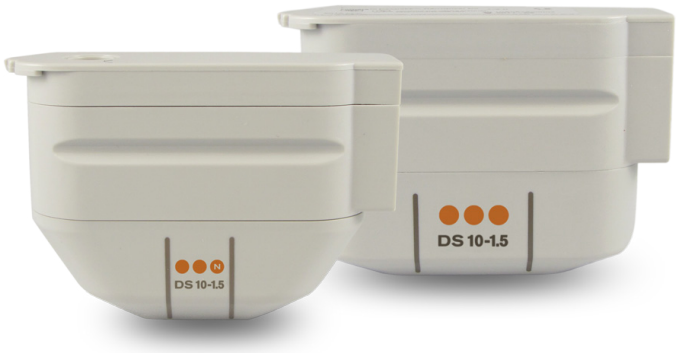
TABLE 1

Pre-release Practice	# Patients Treated	Average # Lines	Immediate Device Adverse Events	Long Term Device Adverse Events
1	10	59	None	None
2	45	45	None	None
3	23	45	Nerve Inflammation-probable-resolved; Dry Peri-Orbital-*possible*-resolved;	Edema-around right lateral orbit-1 ½ M-*definite*-resolved
4	15	145	None	None
5	6	205	None	None
6	4	95	None	None
7	10	145	None	None

CLINICAL STUDIES IN SKIN OF COLOR

Data from previous clinical studies have been published which describe the use of the Ulthera System in patient populations of differing skin types [1-3]. These studies included patients of Korean (n=22) [2] and Chinese (n=49) [3] origin, all of which were Fitzpatrick skin type III-VI. It should be noted that 1-2 small isolated spots of post inflammatory hyperpigmentation (PIH) were noted on two of the Chinese study subjects after treatment on the forehead with the 7.0 MHz/4.5 mm transducer, but was not detected in subsequent treatments after switching to the more superficial 7.0 MHz/3.0 mm transducer for the remaining sessions [3]. Preliminary studies on the effect of bone proximity on the distribution of microfocused ultrasound (MFU) energy has suggested that the distance of MFU energy in relation to bony processes may be important in the predictability of energy placement (unpublished data). This reemphasizes the importance of visualization of the tissue being treated, especially over bony prominences, and adjusting the treatment accordingly. Nevertheless, dyspigmentation has not been reported in any other clinical studies and have never been reported with treatments involving the 7.0 MHz/3.0 mm transducer, which is the most superficial of the transducers previously available.

A recent clinical study has evaluated the use of a 10 MHz/1.5 mm transducer for the treatment of the superficial dermis in the face, submental region and upper neck [4]. In this study, 47% of the study population (n=15) were either Fitzpatrick skin type IV or V. Transducers were selected to target the dermal or subdermal tissues at either 3 mm or 4.5 mm depending on the area of the face (e.g., 3.0 mm for forehead and 4.5 mm for cheeks) per current 5.0 PLUS guidelines. Ultrasound energy was also delivered more superficially, at a depth of 1.5mm over areas of the face targeted by the 3mm and 4.5mm treatment depths. None of the subjects reported with hypo- or hyperpigmentation, and all adverse events were expected, mild and transient. Additionally, treatment with the 1.5 mm transducer did not create or exacerbate melasma in any of the study patients. This data suggests that the 1.5 mm transducer can be used safely and without pigmentation issues, regardless of patient skin type.



1.5MM SHALLOW TRANSDUCER

CONCLUSION

The Ulthera System has been shown to be efficacious in the lifting of the brow, and is quickly becoming a staple among physicians in the medical aesthetics arena. With the addition of the 1.5 mm transducer, Ulthera aims to add further value to its already proven platform. Studies to date have shown Ulthera's superficial transducers (3.0 mm and 1.5 mm) to be safe in patients, even those with skin of color (Fitzpatrick IV-VI). While the clinical data on using the 1.5 mm transducer is still preliminary and the use limited to a relatively small number of practices, Ulthera is optimistic that the availability of the 1.5 mm shallow transducer will allow practitioners to achieve a more complete facial rejuvenation.

SOURCES

1. Alam, M., et al., *Ultrasound tightening of facial and neck skin: a rater-blinded prospective cohort study.* J Am Acad Dermatol, 2010. 62(2): p. 262-9.
2. Suh, D.H., et al., *Intense focused ultrasound tightening in asian skin: clinical and pathologic results.* Dermatol Surg, 2011. 37(11): p. 1595-602.
3. Chan, N.P., et al., *Safety study of transcutaneous focused ultrasound for non-invasive skin tightening in Asians.* Lasers Surg Med, 2011. 43(5): p. 366-75.
4. Data on file