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ORIGINAL ARTICLE

Microfocused ultrasound with visualization: Consensus on safety and review of energy-based devices

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Abstract

Background: Microfocused ultrasound with visualization (MFU-V; Ultherapy®, Merz North America) is US Food and Drug Administration-cleared as a non-invasive procedure that lifts the soft tissue of the neck, submentum and brow, and improves lines and wrinkles on the upper chest. Several other energy-based devices are in use in countries outside the USA where they are marketed for indications similar to those of MFU-V, although published studies supporting these indications are limited and none of the other devices provides visualization or verification they reach the superficial musculoaponeurotic system.

Methods: Due to the evolving landscape of ultrasound technology as more devices enter the market, seven global thought leaders who are qualified experts on the use of various high-intensity focused ultrasound (HIFU)/MFU-V technologies convened to review data from an independent evaluation of the software, thermal characteristics, transducer acoustics and ultrasound therapy of MFU-V and three other ultrasound-based devices.

Results: The independent testing demonstrated the devices have key differences in several parameters that play a role in safety and effectiveness. Specifically, MFU-V has visualization capability but the other devices lack that feature. Other differences include the retention of patient history, consistent size and uniformity of thermal coagulation points (TCPs), precise localization of energy concentration at the focal point, and reliable thermal regulation during use. The expert panel established a consensus on the types of preventable complications associated with ultrasound-based energy devices and techniques for preventing and treating complications.

Conclusions: The independent test results of MFU-V/HIFU devices and the consensus panel conclusions provide strong support that real-time visualization and the capability to detect coupling, features found only in MFU-V, help prevent complications and enhance the safety and effectiveness of energy-based devices. The independent evaluation also revealed that MFU-V has several additional features that play key roles in safety and clinical effectiveness, including uniformity of TCPs, tight thermal regulation, large focal gain, and short beam length, that were not found collectively in any of the HIFU devices.

1 | INTRODUCTION

Microfocused ultrasound with visualization (MFU-V; Ultherapy®, Merz North America) is US Food and Drug Administration-cleared as a non-invasive procedure that lifts the brow, submental (beneath the chin) and neck tissue, and improves lines and wrinkles on the upper chest.[1] The visualization feature of MFU-V enables real-time imaging of tissue layers to a depth of 8 mm, allowing the user to confirm appropriate depth of treatment, avoid treatment of non-target tissue,[1] tailor the focal depth and energy of the emitted ultrasound therapy for individual patients, and detect whether the transducer is properly coupled to the target tissue to allow proper energy delivery. Approximately 50 published clinical studies have confirmed the safe and effective use of MFU-V alone[2–5] and in combination with toxins, fillers, and suspension threads[6–8] for lifting and tightening lax soft tissue. Side effects associated with MFU-V are typically mild and transient.[9,10]

Several other energy-based devices that use high-intensity focused ultrasound (HIFU) are in use in countries outside the USA where they are marketed for indications similar to those of MFU-V, although published studies supporting HIFU use for these indications are limited, and none of the other devices provide visualization. A PubMed search found two publications describing the use of a competing device (Doublo™, Hironic Co., Ltd.) for treating neck and lower facial laxity ($N = 43$)[11]and facial laxity ($N = 11$),[12] one study involving a second device (Ultraformer® III, Classys Inc.) for treating cheeks, lower abdomen and thighs ($N = 32$)[13] and one for a third device (Ultraskin™, Won Tech Co., Ltd.) for treating age-related facial laxity ($N = 28$).[14] The manufacturer of the Doublo device markets it as using HIFU for skin rejuvenation, face lifting, and collagen remodeling.[15] The Ultraformer III manufacturer says the device uses HIFU-powered cartridges as a non-invasive system for lifting, tightening, and contouring.[16] Ultraskin is described by its manufacturer as using HIFU for lifting and tightening of the eyebrows, cheeks, nasolabial folds, fine wrinkles, and submental region.[17]

Due to the evolving landscape of HIFU/MFU-V as more devices enter the market, a panel of seven global thought leaders who are qualified experts on the use of various HIFU/MFU-V technologies convened at the International Master Course on Aging Science on January 29, 2020 in Paris, France. The panel reviewed data generated during a series of prior experiments conducted by an independent firm that evaluated MFU-V and three other energy-based devices that use HIFU. An expert panel of aesthetic physicians previously concluded that MFU-V is the gold standard for nonsurgical soft tissue lifting and tightening.[18] Specifically, the objective of the current expert panel was to better understand the safety concerns associated with energy-based devices and achieve an expert consensus on the prevention and management of treatment-related complications.

2 | METHODS

Prior to the consensus meeting, an independent firm (Design Solutions Inc.) tested four MFU-V or HIFU devices with respect to software, thermal characteristics, transducer/cartridge acoustics, and ultrasound therapy.

The four devices tested consisted of (additional information is provided in Appendix 1):

- Doublo-Gold (Hironic Co., Ltd.; [HIFU-1])
- Ultraformer III (Classys Inc.; [HIFU-2])
- Ultraskin II (Won Tec Co., Ltd.; [HIFU-3])
- Ultherapy (Merz North America; [MFU-V])

Testing protocols used were developed to address aspects of the devices that would be accessed when going through certification testing, such as IEC 60601, IEC 60601237, and IEC 6060112. Testing thresholds were derived from the appropriate international standard(s), and the same thresholds were applied to all devices for comparison. For the thermal coagulation point (TCP) testing, all tests were performed at the default values.

The testing results were reviewed by the consensus group. The consensus group also reviewed case presentations that included topics such as the clinical effectiveness and safety of the devices, the safety and effectiveness of MFU-V compared with that of HIFU, and case reports of potential complications experienced by patients treated with non-visualization HIFU and MFU-V.

A subsequent discussion included how visualization of coupling and target tissues can be used to reduce or prevent complications (such as burns, neurapaxia, bruising, and lipoatrophy), best practices for early identification and management of adverse events, and the development of a consensus on safety factors including prevention, early identification, and management.

The consensus panel voted on four questions regarding the types of preventable complications associated with ultrasound-based energy devices, keys to early recognition of adverse events, techniques for preventing complications, and the most effective management of those complications. Strong consensus was defined as ≥75% agreement, moderate consensus 50% to 74% agreement, and weak consensus <50% agreement.

3 | RESULTS

3.1 | Independent testing: software

A summary of independent test results for device software is presented in Tables 1 and 2. The independent evaluation found that all of the devices–HIFU-1, HIFU-2, HIFU-3, and MFU-V-utilize a touchscreen to interact with the user interface and allow for a similar adjustment of parameters (e.g., line length, energy level, spacing) and the capability to save parameters (Table 1). An access key or lock-out option is available on HIFU-2 and MFU-V but not on HIFU-1 or HIFU-3. All of the devices–HIFU-1, HIFU-2, HIFU-3, and MFU-V–offer treatment line count, transducer line count, and transducer/cartridge information. The independent evaluation found that line tracking per treatment region is not available on HIFU-1, HIFU-2,

TABLE 1 Independent testing: software summary

	HIFU–1[a]	HIFU–2[b]	HIFU–3[c]	MFU-V[d]
Touchscreen	+	+	+	+
Access key	–	+	–	+
Parameter adjustment	+	+	+	+
Save parameters	+	+	+	+
Treatment line count	+	+	+	+
Transducer/Cartridge line count	+	+	+	+
Transducer/Cartridge information	+	+	+	+
Treatment regions	–	–	–	+
Imaging capabilities	–	–	–	+
Imaging records	–	–	–	+
Patient information	–	–	–	+
Patient records	–	–	–	+
Treatment records	–	–	–	+
Facility information	–	–	–	+
Export to USB capable	?	–	?	+

?: It was not clear from the independent testing results whether the device provided this capability.
[a]Doublo-Gold (Hironic Co., Ltd.).
[b]Ultraformer III (Classys Inc.).
[c]Ultraskin II (Won Tec Co., Ltd.).
[d]Ultherapy® (Merz North America).

or HIFU-3, but it is an option an MFU-V. Storage of treatment details, including imaging records, patient information, patient records, treatment records, and the facility information, is not offered on HIFU-1, HIFU-2, and HIFU-3. MFU-V has the capability to retain all of those treatment details.

HIFU-1, HIFU-2, and HIFU-3 do not indicate whether the type of energy used is acoustic or electrical. MFU-V displays acoustic energy. Regarding the spacing of TCPs, HIFU-1's defaults are 1.5 mm on its D4 and L4 cartridges and 1.2 mm on its M7 and S7 cartridges; HIFU-2 and HIFU-3 allow for 1.5 mm on all their cartridges; and MFU-V allows for 1.5 mm on its 4–4.5 and 7–4.5 transducers and 1.1 mm on its 7–3.0 and 10–1.5 transducers (Table 2).

3.2 | Independent testing: thermal characteristics

A summary of independent test results for device thermal characteristics is presented in Table 3. During independent testing, each device was programmed to continuously fire treatment lines for 30 min at the maximum allowable pulse repetition rate for the device under test, while temperatures were measured on the handpiece and the patient contact surface on the transducer/cartridge; per the testing protocol, temperature thresholds were specified to stay below 43°C for patient temperature and 48°C for operator temperature and the devices were assessed for their ability to limit temperature elevation to less than 10°C. All of HIFU-1's cartridges showed a temperature increase of ≥10°C. The L4 cartridge reached a maximum temperature of 54.9°C, exceeding the 43°C patient temperature threshold in the testing protocol. The device only faulted for excessive handpiece temperature. HIFU-2 showed a temperature increase of ≥10°C for 5 of the 7 cartridges tested. The M13 cartridge reached a maximum temperature of 63.4°C (which is above the 43°C patient temperature threshold in the testing protocol), without triggering a fault control. Both the transducers/cartridges and handpieces of HIFU-3 and MFU-V rose less than 10°C during testing and no transducers/cartridges in either device exceeded the 43°C patient temperature threshold. The maximum temperature reached in a HIFU-3 cartridge was 28.6°C in the 7M-3.0 cartridge, an increase of 7.3°C. The maximum temperature in MFU-V transducer was 26.9°C in the 4–4.5 transducer, an increase of 1.1°C.

The device temperature increases correlated with amount of power draw observed during electrical tests (Figure 1). HIFU-1's power draw ranged from 56.9 VA for the cartridge with the lowest maximum temperature to 119.5 VA for the cartridge with the highest maximum temperature. HIFU-2's range was from 113.6 VA to 356.7 VA. HIFU-3 and MFU-V transducers each had virtually identical power draws with no large temperature increases. HIFU-3's power draw ranged from 89.1 VA to 98.7 VA. MFU-V ranged from 85.7 VA to 86.1 VA.

3.3 | Independent testing: transducer/cartridge acoustics

A summary of independent test results for device operating area and focal gain is presented in Table 4. Focal gain is a measure of the concentration of acoustic pressure at the focal point compared to the acoustic pressure at the transducer/cartridge surface. HIFU-1's focal gain

TABLE 2 Independent testing: software treatment parameters

Parameter	HIFU–1[a]				HIFU–2[b]							HIFU–3[c]		MFU-V[d]			
Transducer/ Cartridge	D4	M7	S7	L4	L4-4.5	L7-3.0	L7-1.5	M2	M6	M9	M13	4M–4.5	7M–3.0	4–4.5	7–3.0	7–4.5	10–1.5
Default energy (J)	2.00	0.45	0.20	2.00	0.7	0.5	0.2	0.1	1.5	1.5	1.5	1.2[e]	0.8[e]	0.90	0.30	0.75	0.18
TCP[f] spacing (mm)	1.5	1.2	1.2	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.1	1.5	1.1

[a]Doublo-Gold (Hironic Co., Ltd.).

[b]Ultraformer III (Classys Inc.).

[c]Ultraskin II (Won Tec Co., Ltd.).

[d]Ultherapy® (Merz North America).

[e]J/cm^2.

[f]Thermal Coagulation Points.

TABLE 3 Independent testing: temperature changes

Parameter	HIFU–1[a]				HIFU–2[b]							HIFU–3[c]		MFU-V[d]			
Transducer/Cartridge	D4	M7	S7	L4	L4-4.5	L7-3.0	L7-1.5	M2	M6	M9	M13	4M–4.5	7M–3.0	4–4.5	7–3.0	7–4.5	10–1.5
Maximum transducer/Cartridge temperature, °C	45.0	38.6	31.4	54.9	49.6	44.1	31.7	30.4	58.4	61.7	63.4	25.8	28.6	26.9	25.6	26.7	25.7
Transducer/Cartridge temperature increase, °C	20.5	17.0	10.2	32.5	27.3	12.9	7.5	6.6	35.5	37.7	40.4	4.0	7.3	1.1	0.8	1.1	1.0
Maximum handpiece temperature, °C	31.1	30.5	29.5	29.7	31.9	32.5	30.7	31.5	31.3	31.3	31.3	28.4	28.2	31.0	29.8	31.3	29.5
Handpiece temperature increase, °C	4.0	6.3	6.5	4.1	9.1	4.5	6.6	5.9	5.6	5.6	6.9	1.9	5.7	5.2	4.6	6.0	4.4

[a]Doublo-Gold (Hironic Co., Ltd.).

[b]Ultraformer III (Classys Inc.).

[c]Ultraskin II (Won Tec Co., Ltd.).

[d]Ultherapy® (Merz North America).

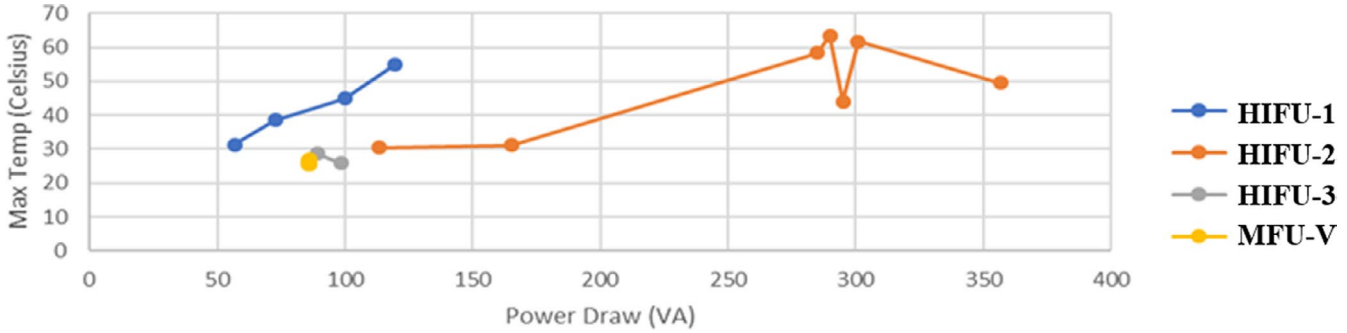

FIGURE 1 Independent testing: ultrasound power draw vs. max transducer temperature plot

ranged from 20.9 to 72.9, HIFU-2 ranged from 28.0 to 69.4, HIFU-3 ranged from 25.5 to 44.5, and MFU-V ranged from 62.2 to 139.49.

The measured operating frequency of the ultrasonic signal of the device's transducers/cartridges varied from the expected frequencies listed in the device labels and manuals (Table 5). HIFU-1's variance from nominal frequency ranged from 2.9% to 20.0% with a maximum measured frequency of 7.3 MHz. HIFU-2's variance ranged from −24.3% to 10.0% with a maximum measured frequency of 5.5 MHz. HIFU-3 differed from nominal frequency by 0.0% to 5.0% and achieved a maximum measured frequency of 7.0 MHz. MFU-V's variance was from −1.0% to 10.0% and its maximum measured frequency was 9.9 MHz.

A summary of independent test results for beam dimension is presented in Table 6. The beam dimension evaluation included beam depth (analogous to focal depth), azimuth (the width of the beam at each treatment spot), and elevation (height at each treatment spot). Beam depth ranged from 1.37 to 4.17 mm for HIFU-1, 1.00 to 3.71 mm for HIFU-2, 2.08 to 2.62 mm for HIFU-3, and 0.75 to 1.64 mm for MFU-V. HIFU-1's beam azimuth range was 0.22 to 0.58 mm, HIFU-2's was 0.19 to 0.62 mm, HIFU-3's was 0.33 to 0.39mm, and MFU-V's was 0.13 to 0.28 mm. Beam elevation was 0.23 to 0.57 mm for HIFU-1, 0.29 to 0.61 mm for HIFU-2, 0.32 to 0.34 mm for HIFU-3, and 0.12 to 0.31 mm for MFU-V.

3.4 | Independent testing: ultrasound therapy

The overall uniformity of lesions produced by the devices was evaluated by treating into a polybutadiene rubber-based tissue-mimicking material (Figure 2). This clear and colorless tissue-mimicking material becomes opaque when treated with HIFU. The opaque regions may be analyzed for size, shape, and position to infer TCP volumes and uniformity. HIFU-1 lesions produced by its D4-4.5 cartridge measured 0.241–0.344 mm (Figure 2A, top view) and 0.77 x 0.29 mm and 0.64 x 0.29 mm (Figure 2A, side view). Lesions produced by HIFU-2's L4 M-4.5 cartridge were 0.28–0.29 mm (top view) and 1.43 x 0.38 mm and 1.96 x 0.38 mm (side view). HIFU-3's L4M-4.5 cartridge produced lesions that measured 0.15–0.16 mm (top view) and 0.49 x 0.21 mm and 0.59 x 0.20 mm (side view). MFU-V's DS 4–4.5 lesions were 0.21–0.21 mm (top view) and 0.52 x 0.37 mm and 0.52 x 0.36 mm (side view).

Lesions produced by HIFU-1's M7-3.0 cartridge measured 0.65–0.66 mm (Figure 2B, top view) and 1.98 x 0.82 mm and 2.04 x 0.92 mm (Figure 2B, side view). HIFU-2's L7-3.0 lesions ranged from 0.34–0.37 mm (top view) and 1.07 x 0.27 mm and 1.15 x 0.22 mm (side view). HIFU-3's 7M-3.0 lesions measured 0.19–0.20 mm (top view) and 0.62 x 0.20 mm and 0.51 x 0.17 mm (side view). MFU-V's DS 7–3.0 transducer produced lesions that were 0.25–0.26 mm (top view) and 0.36 x 0.33 mm and 0.31 x 0.32 mm (side view).

3.5 | Independent testing: visualization

The independent evaluation found that HIFU-1, HIFU-2, and HIFU-3 do not have the capability to provide real-time imaging during treatment and cannot detect sufficient coupling. MFU-V has imaging capabilities that can provide real-time visualization during treatment and is able to detect sufficient coupling. MFU-V also will provide an error code to alert the user if the coupling is not adequate.

3.6 | Case presentations

Several presentations by panel members demonstrated potential injury from ultrasound treatments. Complications included dermal thermal damage (burns/welts/grid lines/scabbing/blisters/tenderness/post-inflammatory hyperpigmentation/purpura/hypochromic lesions/swelling, $N = 17$), vascular damage (bruising, ecchymoses; $N = 10$), fatty layer damage/lipoatrophy ($N = 5$), and neural interaction with heat: neurapraxia/palsy/paresis/numbness ($N = 3$). The consensus panel concluded that many injuries could be prevented if visualization was used. Detailed presentations focused on burns, skin loss, and nerve injury.

3.7 | Consensus outcomes

Results of the panel consensus votes on techniques for preventing complications, types of preventable complications associated with ultrasound-based energy devices, keys to early recognition of

TABLE 4 Independent testing: operating area and focal gain

Parameter	HIFU–1[a]				HIFU–2[b]							HIFU–3[c]		MFU-V[d]			
Transducer/Cartridge	D4	M7	S7	L4	L4-4.5	L7-3.0	L7-1.5	M2	M6	M9	M13	4M–4.5	7M–3.0	4–4.5	7–3.0	7–4.5	10–1.5
Effective transducer/Cartridge area (cm^2)	2.40	1.93	2.29	1.04	3.92	2.43	2.41	2.27	2.71	3.25	4.17	2.75	0.66	3.23	3.37	3.19	3.19
Focal gain	49.2	60.5	72.9	20.9	68.0	69.4	65.9	39.3	28.0	28.9	32.5	44.5	25.5	62.2	106.58	104.29	139.49

[a]Doublo-Gold (Hironic Co., Ltd.).

[b]Ultraformer III (Classys Inc.).

[c]Ultraskin II (Won Tec Co., Ltd.).

[d]Ultherapy® (Merz North America).

TABLE 5 Independent testing: operating frequency[a]

Parameter	HIFU–1[b]				HIFU–2[c]							HIFU–3[d]		MFU-V[e]			
Transducer/Cartridge	D4	M7	S7	L4	L4-4.5	L7-3.0	L7-1.5	M2	M6	M9	M13	4M–4.5	7M–3.0	4–4.5	7–3.0	7–4.5	10–1.5
Expected frequency (MHz)	4.0	7.0	7.0	4.0	4.0	7.0	7.0	5.5	2.0	2.0	2.0	4.0	7.0	4.0	7.0	7.0	10.0
Measured frequency (MHz)	4.8	7.2	7.3	4.7	3.9	5.5	5.3	5.1	2.2	2.2	2.1	4.2	7.0	4.4	7.3	7.4	9.9
% Diff from nominal	20.0	2.9	4.3	17.5	−2.5	−21.4	−24.3	−7.3	10.0	10.0	5.0	5.0	0.0	10.0	4.3	5.7	−1.0

[a]The measured operating frequency is the frequency of an ultrasonic signal based on the observation output of a hydrophone in the ultrasonic field. This parameter is measured in MHz. 1 MHz corresponds to a period of 1 μs for each wave.

[b]Doublo-Gold (Hironic Co., Ltd.).

[c]Ultraformer III (Classys Inc.).

[d]Ultraskin II (Won Tec Co., Ltd.).

[e]Ultherapy® (Merz North America).

TABLE 6 Independent testing: beam dimension

Parameter	HIFU-1[a]				HIFU-2[b]					HIFU-3[c]		MFU-V[d]			
Transducer/Cartridge	D4	M7	S7	L4	L4-4.5	L7-3.0	L7-1.5	M2	M6	M9	M13	4M–4.5	7M–3.0	4–4.5	7–3.0	7–4.5	10–1.5
Depth/z-axis[e] (mm)	2.01	1.51	1.37	4.17	1.45	1.01	1.00	2.45	3.29	3.69	3.71	2.08	2.62	1.64	0.98	0.96	0.75
Azimuth/x-axis[f] (mm)	0.33	0.22	0.23	0.58	0.26	0.19	0.21	0.33	0.57	0.57	0.62	0.39	0.33	0.28	0.18	0.18	0.13
Elevation/z-axis[g] (mm)	0.28	0.25	0.23	0.57	0.43	0.29	0.32	0.47	0.57	0.61	0.57	0.34	0.32	0.31	0.18	0.17	0.12

[a]Doublo-Gold (Hironic Co., Ltd.).
[b]Ultraformer III (Classys Inc.).
[c]Ultraskin II (Won Tec Co., Ltd.).
[d]Ultherapy® (Merz North America).
[e]Beam depth is the distance along the beam axis containing the peak rarefactional pressure. This is analogous to focal depth as this is the measured depth of the highest energy of the ultrasound field.
[f]Beam azimuth is the beam width at the measured beam depth or treatment spot. The width is defined as the distance where the pressure squared integral falls by 6 dB from the peak.
[g]Beam elevation or height at each treatment spot is the distance in the elevation direction where the pressure squared integral falls by 6 dB from the peak.

adverse events, and the most effective management of complications are summarized in Table 7. Further details about the questions and responses are provided in Appendix 2.

4 | DISCUSSION

The objective of each device is to use thermal energy to stimulate the body's natural wound-healing process. The degree of clinical effectiveness and safety is related to a device's capability to precisely and consistently elevate tissue temperatures to achieve coagulation while leaving nontarget tissue undisturbed. The independent testing demonstrated the devices evaluated have differences in several parameters that play a role in safety and effectiveness, including visualization, software capabilities, thermal characteristics, and transducer/cartridge acoustics.

Visualization is a key area where the devices differed. Visualization enhances safety and effectiveness because it enables energy to be delivered precisely and accurately,[1,19] it permits confirmation of the depth of treatment to target specific foundational tissues where laxity begins,[1,19] and it allows for a customized procedure for each patient.[2,20] Real-time visualization allows for confirming the device is properly positioned against the skin surface, which ensures safe transfer of energy.[18] This also permits the clinician to visualize the intended treatment area and avoid treating bone, large blood vessels, or other non-target tissues and helps determine the depth of the SMAS and dermal layer, which may influence the choice of transducer/cartridge and number of lines at each targeted depth depending on the intended outcome.[18] MFU-V is the only device tested that provides imaging capability. HIFU-1, HIFU-2, and HIFU-3 lack that feature.

Patient safety should take priority. The presented cases demonstrate various complications, including welts, blistering, burn, and scarring, that have occurred in patients treated with devices that lacked visualization. The panel reached strong consensus that visualization could help prevent these and other complications that can occur with ultrasound-based energy devices, such as grid lines, swelling, neurapraxia/palsy/paresis/numbness, tenderness, bruising, pain, post-inflammatory hyperpigmentation, ecchymoses, fatty layer damage/lipoatrophy, and scabbing. This is in line with previous evaluations that found that when MFU-V is used properly, most adverse effects can be avoided and those that do occur are typically mild, transient, and resolve without sequelae.[9,10]

The independent evaluation found the devices varied in several software features, including the spacing of TCPs. Inconsistent size and formation of TCPs can result in ineffective treatment.[21] Optimally-focused TCPs may enhance the amount of healthy tissue between TCPs, stimulating neocollagenesis by triggering the natural healing process, resulting in gradual collagen and elastin production.[1,22] MFU-V default settings allow for spacing of TCPs down to 1.1 mm, which is the smallest default TCP spacing setting of the devices tested. In the tissue-mimicking material analysis, the overall uniformity of the lesion shapes produced by the MFU-V system appears qualitatively

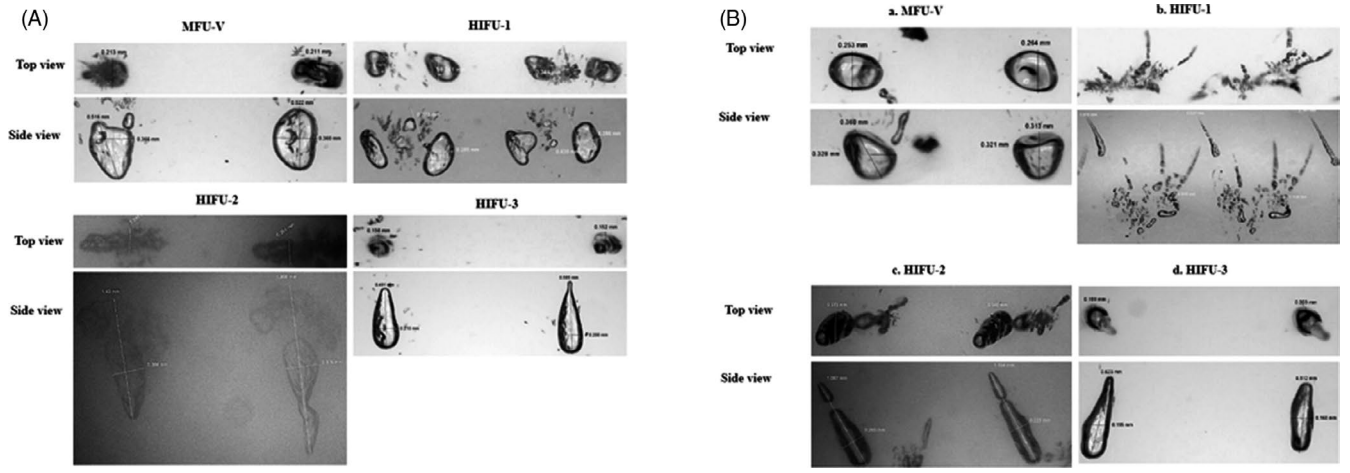

FIGURE 2 Independent testing: tissue-mimicking material analysis. (A) Lesions produced during tissue-mimicking material analysis using the DS 4–4.5, D4-4.5, 4M-4.5, and L4-4.5 transducers/cartridges with MFU-V, HIFU-1, HIFU-2, and HIFU-3 devices, respectively. (B) Lesions produced during tissue-mimicking material analysis using the DS 7–3.0, M7-3.0, L7-3.0, and 7M-3.0 transducers/cartridges with MFU-V, HIFU-1, HIFU-2, and HIFU-3 devices, respectively

more consistent than the lesions produced by HIFU-1 and HIFU-2 and equivalent in consistency to the lesions produced by HIFU-3. In comparison with the other devices, HIFU-1 produced lesions within the tissue-mimicking material with the greatest qualitative variability.

Other software differences between the devices included: the retention of pertinent patient and treatment data, which allows for easy tracking of treatment progress and establishment of a patient history, and display of acoustic energy, which permits the operator to access the efficiency of the transducer/cartridge. MFU-V's software offers all of those features. HIFU-1, HIFU-2, and HIFU-3 do not include those in their software options.

Another software difference between the devices was the availability of a lock-out method or access key. Without this option, devices could be vulnerable to unauthorized use and misuse. HIFU-2 and MFU-V offer an access key or lock-out option. HIFU-1 and HIFU-3 do not have that capability.

The devices differed in their thermal control or ability to remain cool and not exhibit spikes in temperature and power draw. Excessive transducer heat can change the transducer's/cartridge's acoustic performance and resonance behavior, resulting in inefficient therapeutic output, and higher device temperature can cause undue wear of the electronic components. Excessive increases in transducer/cartridge temperature and ineffective fault trigger increases the risk of complications in the patient, such as skin burns with hyperpigmentation[23] and prolonged recovery time, could prevent treatment completion, and also poses a hazard to the operator. HIFU-1 and HIFU-2 displayed a wide range of power draws and excessive temperature increases in their cartridges. HIFU-2 also had an ineffective fault trigger, permitting one cartridge to exceed the patient temperature threshold. HIFU-3 did not display an excessive temperature increase during testing and also maintained a steady power draw. MFU-V transducers had virtually identical power draws with no significant temperature increases, which could enable operators to provide longer or consecutive treatments.

The independent testing also revealed differences in transducer/cartridge acoustics between the devices, including focal gain, operating frequency, and beam dimension. A larger focal gain or localization of the energy concentration at the focal point is important for preventing surrounding tissues from becoming unduly heated whereas a lower focal gain could result in reduced heating rates, effectiveness, and the chance of creating impactful TCPs. HIFU-1, HIFU-2, and HIFU-3 had a lower focal gain overall than MFU-V.

A higher operating frequency permits a wider range of frequency options and facilitates the tailoring of treatment to meet the specific needs or desired outcomes of individual patients. MFU-V had the highest maximum measured operating frequency (9.9 MHz) followed by HIFU-1 (7.3 MHz), HIFU-3 (7.0 MHz), and HIFU-2 (5.5 MHz). MFU-V also utilizes transducers of different frequencies that permit tissue heating at depths of 1.5, 3.0, and 4.5 mm, targeting the mid-dermal, deep dermal, superficial subcutaneous, and fibromuscular planes.[1]

A longer beam may increase the risk for surface welts and blisters if given with sufficient power. HIFU-1, HIFU-2, and HIFU-3 had a longer beam for the 1.5 mm treatment depth than MFU-V.

The independent analysis, particularly the thermal control and focal gain results, indicates a difference in efficiency between the devices. The efficiency of the device during treatment is an important concern because it could affect patient safety. To achieve the same effect as a single treatment from a more efficient device, treatment with less efficient devices potentially may require several treatments, increasing exposure and the risk of complications. Consistent with this, a recent review noted that protocols for MFU-V for noninvasive lifting call for one treatment annually whereas protocols for HIFU devices advise 3–4 treatments per year, an indication that efficacy does not persist as long.[21] In addition, an extensive body of evidence consisting of more than 50 peer-reviewed clinical studies supports the safety and efficacy of MFU-V while there is a paucity of published studies involving HIFU-1, HIFU-2, or HIFU-3 (Appendix 1).

TABLE 7 Consensus questions

Response	Respondents/consensus strength
Question 1: Please provide your approaches and techniques for preventing complications when delivering ultrasound-based energy.	
Visualization	7/Strong
Anatomical understanding	7/Strong
Good coupling/correct amount of gel/correct pressure	7/Strong
Exact mapping/marking/plan/diagnostic	6/Strong
Detailed medical history	7/Strong
Facial examination/ skin thickness	6/Strong
Pain threshold/setting pain expectations/ avoiding excessive pain/ pain monitoring	7/Strong
Good training	7/Strong
Selective test patch (assess skin reaction)/diagnostic lines	4/Moderate
Question 2: What types of preventable complications have you seen, or you believe could happen with ultrasound-based energy devices without visualization?	
Dermal thermal damage: burns/welts/grid lines/scabbing/blisters/ tenderness/post-inflammatory hyperpigmentation/purpura/hypochromic lesions/swelling	7/Strong
Neural interaction with heat: neurapraxia/palsy/paresis/numbness	7/Strong
Vascular: bruising, ecchymoses	7/Strong
Parotitis	7/Strong
Fatty layer damage/lipoatrophy	7/Strong
Question 3: If these issue(s) arise, what are the keys to early recognition?	
Severe/unexpected pain	7/Strong
Dermal damage: Unexpected or prolonged redness (>24 h)/localized swelling/welts	7/Strong
Brow ptosis/asymmetric smile (smile and whistle test) (immediate or delayed)	7/Strong
Question 4: What would be your approach for the most effective management of dermal burns/welts/grid lines/redness/swelling (>24 h)?	
Topical steroids	7/Strong
Topical/oral antibiotics/cefaclor 100 mg BID for 5 days	0/Not recommended (unless necrotic tissue; then antiseptics/silver sulfadiazine/ antimicrobial dressing and no steroids)
Systemic steroids	0/Not recommended
Question 5: What would be your approach for the most effective management of neurapraxia/palsy/paresis/numbness?	
Oral steroids	6/Strong
Botulinum toxin to correct asymmetries (DAO only)	6/Strong (case-dependent, ≥2 weeks)
B vitamins or other supplement	5/Moderate

The analysis described here included ultrasound devices that were available on the market at the time of the consensus. Other ultrasound devices were not available for independent testing or consensus panel review and have not been included in the devices tested here.

5 | CONCLUSION

The independent test results of MFU-V/HIFU devices and the consensus panel conclusions provide strong support that real-time visualization and the capability to detect coupling, features found in MFU-V but not the HIFU devices, help prevent complications and enhance the safety and effectiveness of energy-based devices. The independent evaluation also revealed that several additional parameters that play key roles in safety and clinical effectiveness, including uniformity of TCPs, tight thermal regulation, large focal gain and short beam length, are provided by MFU-V but they were not found collectively in any of the HIFU devices.

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DISCLOSURE

This activity was sponsored by Merz Aesthetics, Raleigh, NC. T. Pavicic has acted as a speaker and advisor for Merz Aesthetics, BTL, Lutronic, AAT, and Johnson & Johnson; she has conducted clinical trials for Merz Aesthetics, AAT, and LG. T.B., N.C., C.H., J.P., A.S., J.S.,

and S.V. have been consultants and/or speakers for Merz Aesthetics. J.R. Ballard's involvement was limited to the independent testing of the devices. He was not involved in the panel evaluation of the results or the consensus discussions.

AUTHOR CONTRIBUTIONS

All authors have read and approved the final manuscript. J.R.B. designed, conducted, and analyzed the independent testing research. T.P. chaired the consensus meeting and T.B., N.C., C.H., J.P., A.S., J.S., and S.V. participated in the expert consensus panel meeting. All authors participated in the clinical interpretation of the data for the manuscript and consensus. The authors acknowledge the editorial assistance of Emma Robertson, Dr. Carl S. Hornfeldt, Apothekon, Inc., and Steve Mitchell during the preparation of this manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICAL APPROVAL

No ethical approval was required as this research did not involve human subjects or animals.

ENDNOTE

[1] CE-marking (Conformité Européenne) signifies products sold in the European Economic Area (EEA) have been assessed to meet high safety, health, and environmental protection requirements. CE marking also supports fair competition by holding all companies accountable to the same rules. By affixing the CE marking to a product, a manufacturer declares that the product meets all the legal requirements for CE marking and can be sold throughout the EEA.

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APPENDIX 1

MFU-V

Ultherapy® (Merz North America, Raleigh, NC, USA).

CE-Marked: Yes.

Indication: Lift the eyebrow, lift lax submental (beneath the chin) and neck tissue, and improve lines and wrinkles of the décolletée.

DeepSEE® (Merz Aesthetics; Raleigh, NC).

CE-Marked[1]: Yes.

Indication: Ensure proper coupling of the transducer to the skin and confirm appropriate depth of treatment such as to avoid bone.

Technology: Microfocused ultrasound with visualization.

Product Website: https://ultherapy.com/

Publications: ~50.

HIFU-1

Doublo-Gold [CE-Marked][1] (Hironic Co., Ltd., Yongin-si, South Korea).

CE-Marked: Yes.

Indication: Axillary hyperhidrosis.

Doublo-Gold [non-CE-Marked] (Hironic Co., Ltd., Yongin-si, South Korea).

CE-Marked: No.

Indications: Skin rejuvenation, face lifting, wrinkle treatment.

Technology: High-intensity focused ultrasound.

Product Website: https://hironic.com/p/doublo-gold

Publications: Two studies involving Doublo.[11,12] None involving Doublo-Gold.

HIFU-2

Ultraformer III (Classys Inc., Seoul, South Korea).

CE-Marked: Yes.

Indication Unclear: "Non-invasive system for lifting, tightening & contouring".

Technology: Micro- and macrofocused ultrasound.

Product Website: https://ultraformer.com/

Publications: One[13]

HIFU-3

Ultraskin II (Won Tec Co., Ltd., Daejeon, South Korea).

CE-Marked: Yes.

Indication: Lifting and tightening of the eyebrows, cheeks, nasolabial folds, fine wrinkles, eye lifting, and submental region.

Technology: High-intensity focused ultrasound.

Product Website: http://www.wtlaser.com/en/sub/company/contact-us.asp

Publications: One study involving Ultraskin.[14] None involving Ultraskin II.

APPENDIX 2

WORKSHOP DISCUSSION

The following questions were provided to consensus panel members prior to the meeting. Their responses are listed after each question.

Please provide your approaches and techniques for preventing complications when delivering ultrasound-based energy.

Responses included visualization ($n = 4$), anatomical understanding/avoiding "no-go" areas ($n = 3$), good coupling ($n = 3$), correct amount of gel ($n = 2$), exact mapping/marking ($n = 2$), detailed medical history ($n = 2$), diagnostic "test lines" ($n = 2$), good training ($n = 2$) and other (for each, $n = 1$) including short treatments, test spot (acryl plate), facial examination, avoid overlapping, avoid combination with dermal-targeting procedures at same time, correct patient selection, analgesia/pain management, pressure applied during treatment to minimize risk of edema and bruising and post-treatment cooling.

What types of preventable complications have you seen, or you believe could happen with ultrasound-based energy devices without visualization?

Responses were burns/welts/grid lines ($n = 5$), swelling ($n = 4$), neurapraxia/palsy/paresis/ numbness ($n = 4$), tenderness ($n = 3$), bruising ($n = 2$), pain ($n = 2$), post-inflammatory hyperpigmentation (PIH) ($n = 2$), ecchymoses ($n = 2$), fatty layer damage/lipoatrophy ($n = 2$), scabbing ($n = 2$), blisters ($n = 2$), and other (for each, $n = 1$) including parotitis, purpura, and hypochromic lesions.

If any of these issue(s) arise, what are the keys to early recognition?

Responses were severe/unexpected pain ($n = 5$), redness ($n = 5$), localized swelling ($n = 4$), immediate appearance of welts ($n = 3$), and brow ptosis/asymmetric smile (smile and whistle test) ($n = 2$).

What would be your approach for the most effective management of each of those issues / complications? Please name the specifics of the treatment suggested including active ingredients, dose, frequency, and duration.

For swelling, responses were cooling ($n = 3$), LED phototherapy (633 & 830 nm; $n = 2$), hydrochlorothiazide 25 mg BID for 3–5 days ($n = 1$). For burns/welts, responses were topical steroids or oral prednisolone 5 mg TID for 5 days ($n = 2$), sun protection ($n = 2$), topical antibiotics oral cefaclor 100 mg BID for 5 days ($n = 2$), cooling cream ($n = 1$), and valaciclovir for lip area ($n = 1$). For redness, responses were cooling ($n = 5$) and LED phototherapy (633 & 830 nm; $n = 2$). For neurapraxia/palsy/paresis, responses were botulinum toxin ($n = 2$), oral steroids ($n = 2$), soft radiofrequency device twice weekly for 2–3 weeks ($n = 1$) and vitamin B_{12} and B_6 supplements.

For bruising, the response was antithrombotic gel 3–4 times daily (n = 1). For tenderness, responses were cooling (n = 2), LED phototherapy (633 & 830 nm; n = 2), oral steroids (n = 2), and anti-inflammatories agents (n = 1).

For pain, responses were more frequent, but shorter, treatment sessions with 100–150 lines per session, ibuprofen/acetaminophen and vibration distractor, local anesthetic nerve block for upper and lower lip, pediatric fentanyl lollipops for panfacial treatment, ibuprofen 800 mg once 30 min prior to treatment, topical anesthetic (for 1.5 mm transducer only), benzocaine 20%/lidocaine base 6%/tetracaine 4% cream applied for 20 min prior to treatment (occlusion increases effectiveness), reduced energy level, comfort management (pressure on contralateral side, positive psychology, heated couch, blankets, dimly lit room, distraction [music/TV], treatment timing).

For PIH, responses were hydroquinone 4% cream daily and superficial peel with fractionated thulium or Nd YAG laser + topical bleaching agent. For fatty layer damage/ lipoatrophy, responses were re-volumization with a hyaluronic acid dermal filler.