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Research Article

New Cooltech Define® Cryoadipolysis Applicators: A Scientific and Comparative Study with Cooltech® Applicators

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Abstract

Objectives: The main objective of this study was to obtain data from cryoadipolysis simulations to evaluate the designs of new applicators, and how changing shape, dimensions and cooling temperature can increase fat loss.

Methods: The cooling dynamics in the skin and fat of three new Cooltech Define® applicator models, were compared to their marketed Cooltech® counterparts, using 3D designs and multiphysics-simulations were carried out with COMSOL Multiphysics®. Cryoadipolysis treatments were recreated and applying different percentages of ischemia. Variables assessed were: Cooling merit parameter, cooling homogeneity, cooling dynamics of skin and fat, the time required to reach crystallization temperatures (set at 10ºC), fat percentage inside the applicators, and time to hypoesthesia.

Results: At 100% ischemia, the new applicators were able to reduce the time to reach 10 ºC by 52-68% and increase the fat reduction percentage by 15-20%. After adjusting the ischemia value, the new applicators had a fat reduction percentage of 49%, 78%, and 74%, while in the previous series were 21%, 25%, and 68%, respectively.

Conclusion: New cryoadipolysis applicators reached lower temperature, higher cooling speed, more homogeneous cooling, faster hypoesthesia, and greater fat reduction. However, further clinical studies to assess the reproducibility of these data would be needed.

Keywords: Apoptosis, adipocyte, cold, cooling, cryolipolysis, computer modeling, lipolysis, multiphysics simulation software, non-invasive fat removal, non-invasive body contouring, reduction, skin barrier, skin physiology/structure

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Cryoadipolysis as a non-invasive procedure for the removal of adipose tissue was first used in 2010 after the FDA approved a cryolipolysis device to reduce fat (K080521). Many investigations, both *in vitro*[1] and on animals,[2] had been conducted in the past to verify its efficacy and safety.[3] Human clinical trials later confirmed that it was a safe technology with minimum pain and fast recovery.[4]

Within the development framework of new Cooltech Define® cryoadipolysis applicators, multiphysics simulation software has proven to be a useful tool, since it offers the possibility to virtually study how prototypes would behave in a real-life situation through a model that includes the resolution of physical equations by finite elements calculation methods. This has already been verified in the previous development of Cooltech® applicators.[4–6]

The main objective of this study was to evaluate the cooling efficacy of the Cooltech Define® applicators through numerical simulations, and show their superiority to the Cooltech® applicators, which implies greater affectation of the fat inside of them, and therefore, it should reduce fat percentage more effectively. Another objective was to show that the design of the applicators can be optimized using a merit parameter, based on the geometrical design of the applicators. Finally, this study also showed the im-

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portance of considering the biological heat in the simulations and the need to perform clinical studies to determine the ischemia associated with each applicator.

Methods

Study Design

This study, conducted at Cocoon Medical laboratories, in Barcelona (Spain), compared the cooling dynamics of several cryoadipolysis applicators in the skin and fat. Comparative analysis was carried out with the Straight, Tight and Double applicator models from the Cooltech® series as well as from the new Cooltech Define® line.

As with the Cooltech® applicators comparative study,[6] all simulations were performed with COMSOL Multiphysics® software, which enables to evaluate the temperature inside the skin and fat, and recreates the response of the new applicator designs in a real-life situation. This is a calculation method by finite elements that allows to solve equations numerically and is especially useful when equations do not have an analytical solution, as in the case of the heat transfer equation used in this study. The software creates a mesh with a finite number of elements in the domains where the equation needs to be solved and solves the equation numerically in each of these elements, gathering all the data for the final result.[6] In the present study, these meshed geometrical domains included biological tissues (skin and fat) and the applicator hand-piece.

In order to recreate each applicator in the simulation, their 3D designs were imported from the Solid Works® software directly into the simulation software (Figs. 1,2). Taking into account the following design parameters: (1) cooling surface, (2) total cavity volume, (3) cavity depth and (4) surface of the applicator's head, which is related with blood perfusion (Table 1), a merit parameter was defined based on the following premises (Fig. 3):

a) The larger the cooling surface, the larger the tissue area affected by the cold.

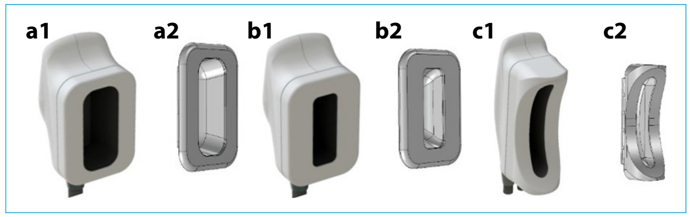

Figure 1. Straight applicator: **(A1)** Simulation design (left) and **(A2)** real image (right). Tight applicator: **(B1)** Simulation design (left) and **(B2)** real image (right). Double applicator: **(C1)** Simulation design (left) and **(C2)** real image (right).

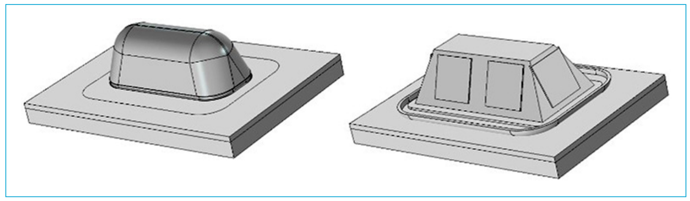

Figure 2. 3D diagram of contact areas between the tissues and the hand piece: to the left, the central zone, representing the tissues that are suctioned inside the applicator (brick of skin and fat) plus the peripheral zone with tissues also affected by the temperature gradient but not suctioned inside the applicator; and to the right, the applicator with the central zone lodged inside plus the peripheral zone.

$$\textit{Merit Parameter} = \frac{\textit{Cooling Surface} \times \textit{Depth}}{\textit{Cavity Volume} \times \textit{Perfusion Surface}}$$

Figure 3. Equation for the merit parameter.

b) The deeper the applicator can reach, the further the tissue will be from the source of biological heat of the body.

c) The lower the volume, the smaller the amount of tissue to cool and, therefore, the larger the cooling capacity.

d) The smaller the blood perfusion surface (applicator entrance surface, through which blood flows to the tissue located inside the applicator), the lower the heating of the tissue inside the applicator.

Regarding the designs imported from the Solid Works® soft-

Table 1. Design parameters of the Cooltech® and Cooltech Define® applicators

Series	Applicator Model	Cooling Surface (cm^2)	Total Cavity Volume (cm^3)	Depth (mm)	Blood Perfusion Surface (cm^2)
Cooltech Define®	Tight	132	177	42	56
Cooltech®		108	309	74	85.2
Cooltech Define®	Straight	180	295	48	84
Cooltech®		106	430	73	111
Cooltech Define®	Double	468	546	54	112
Cooltech®		255	686	73	138

cm^2: square centimeters; cm^3: cubic centimeters; mm: millimeters.

ware, a 3D heat transfer model was used including all materials, from the biological tissues of interest for the simulation (skin and fat) to temperature-based parameters. The inclusion of the design of the applicator hand-piece in the simulation represented an analysis improvement with respect to other studies that only modeled skin and fat volume.[7]

The simulation was carried out by solving the equation of heat transfer for biomaterials (Fig. 4), where ρ is the density of the tissue, C_p is the specific heat capacity of the tissue at constant pressure, k is the thermal conductivity, T is the absolute temperature of the tissue, q is the heat flux by conduction in the tissue, ρ_b is the blood density, $C_{p,b}$ is the blood-specific heat capacity at constant pressure, ω_b is the blood perfusion rate, T_b is the arterial blood temperature, Q_{met} is the metabolic heat source and Q is the heat source, ∇ is the mathematical operator Nabla, and $\partial T/\partial t$ is the partial derivative of temperature with respect to time.

For each material used in the simulation, three basic parameters were required: (1) specific heat *(C_p)*, (2) thermal conductivity *(k)*, and (3) density *(ρ)* (Table 2). Materials used in the simulations were fat,[8] skin,[9] the polypropylene of the applicator outer body,[7] the anodized aluminum of the surface of the cooling plates,[10] and the aluminum of the

$$\rho C_p \frac{\partial T}{\partial t} + \nabla \cdot q = Q + Q_{bio}$$

A. $q = -k\nabla T$

B. $Q_{bio} = \rho_b C_{pb} \omega_b (T_b - T) + Q_{met}$

Figure 4. Equation of heat transfer for biomaterials. **A**: Heat flux by conduction in the tissue. **B**: Biological heat.

ρ: density of the tissue; C_p: specific heat at constant pressure of the tissue; ∂T/∂t: Partial derivative of the temperature *(T)* with respect to the time *(t)*; ∇: mathematical operator Nabla (operator that applies partial derivatives in space to a magnitude); *q*: heat flux by conduction in the tissue; *Q*: heat source; Q_{bio} biological heat; *k*: coefficient of heat conductivity; ρ_b: blood density; $C_{p,b}$: blood specific heat at constant pressure; ω_b: blood perfusion rate; T_b: arterial blood temperature; Q_{met}; metabolic heat source.

cooling plates.[9] In the fat, these three parameters depend on temperature.

Biological heat (Q_{bio}) represents a combination of blood perfusion (or blood flow) and the metabolic heat of each tissue (Fig. 4).[11] It is known that metabolic heat can be considered negligible as a first approximation for protective tissues, like normal skin or subcutaneous fat.[12] Moreover, previous studies also using COMSOL® have demonstrated that changes in metabolic heat do not substantially change the results of the simulation.[13] Therefore, only blood perfusion has been considered in this study to determine biological heat. To simulate blood perfusion, four parameters were needed: (1) blood temperature (T_b), (2) blood-specific heat capacity ($C_{p,b}$), (3) blood density (ρ_b) and (4) blood perfusion rate (ω_b) in fat and the skin[13,14] (Table 3).

No phase change for fat has been introduced in the simulation. In heterogeneous materials like fat, which is composed by several types of different fatty acids, there is not a visible phase change as occurs with water, for example. In a previous study with olive oil-which is known to have a similar chemical composition to human fat-there was not a clear phase change when it was cooled.[5] However, there was a visible increase in viscosity as the temperature decreased.[4] Previous simulations during the refinement of the model showed that results with and without considering phase changes did not have any significant differences.

Recreating the Procedure

The different stages of a cryoadipolysis treatment were

Table 3. Required physical parameters to simulate blood perfusion

Blood Temperature	36 (°C)
C_p blood[14]	3220 (J/kg·K)
ρ blood[14]	900 (kg/m3)
ω in fat[13]	4.2·10-4 (1/s)
ω in the skin[13]	0.0018 (1/s)

°C: degrees Celsius; C_p: specific heat; J: joules; Kg: kilograms; ρ: density; ω: perfusion; m³: cubic meters; s: seconds.

Table 2. Required physical parameters to solve the equation of heat transfer.

Material	Cp (J/kg·K)	k (W/m·K)	ρ (kg/m³)
Fat[8] *T in °C	1984.2+1.4733T -4.8008·10⁻³T²	0.18071-2.7604T ·10⁻⁴-1.7749 ·10⁻⁷T²	925.59-0.41757T
Skin[9]	3391	0.37	1109
Plastic (Polypropylene)[7]	1800	0.16	1040
Anodized aluminum[10]	880	18	2700
Aluminum[9]	900	238	2700

Cp: specific heat; J: joules; Kg: kilograms; K: Kelvin; k: thermal conductivity; W: watts; m: meters; ρ: density; m³: cubic meters; T: temperature; °C: degrees Celsius.

recreated with the simulations, including cooling of tissues by contact with cooled aluminum plates, the use of cryoprotectant on the skin, and the ischemia produced by suction of the tissues inside the applicators.

Regarding the original conditions of the simulations, the initial temperature was 36 ºC for the biological tissue (simulating body temperature), and 20 ºC (room temperature) for the rest of the materials. As a first boundary condition, an isolated system was considered, which means that there was no heat flow in its contours. As a second boundary condition to simulate the cooling process, aluminum plates were at a constant cold temperature for 70 minutes. This boundary condition assumes that aluminum plates, which are cooled in a real-life situation by Peltier cells, reach a cold temperature instantaneously (Fig. 5). Despite this assumption, experimental data showed that several minutes are needed to reach a cold temperature, which then remains constant throughout the treatment thanks to an electronic control system.[15] The temperature was set at -8 ºC for Cooltech® applicators and at -10 ºC for the new Cooltech Define® applicators.

Likewise, it is known that applying cold on the skin causes a marked decrease in sensitivity to pain or hypoesthesia.[16] It is important to reach this state as soon as possible because it makes the treatment painless for patients and gives them more comfort.[17] At 7 ºC, there is numbness in the treated area due to an affectation of the sensory receptors, and at 0 ºC, there is total numbness in the treated area.[2] Other temperatures of interest are: (1) -5 ºC, temperature at which blood vessels start to be affected with thermal damage;[18] (2) -10 ºC, when skin suffers necrosis;[19] and (3) -20 ºC, temperature from which necrosis occurs in any biological tissue.[18,19] Both in the case of Cooltech® and Cooltech Define® applicators, the treated tissue cannot reach temperatures under -20 ºC, but it is possible for blood vessels to reach -5 ºC and for the skin to reach -10 ºC. For this reason, in order to protect tissues from inherent damage by freezing, a cryoprotectant membrane, Cool Gel Pad® [product associated with patent applications: 2018/060533 A1 and PCT/ES2018/070185], is applied.[20]

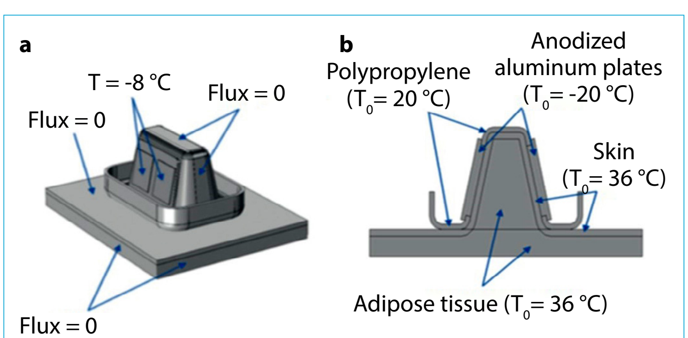

Figure 5. Boundary conditions **(A)** and initial conditions **(B)** used. Abbreviations: T, temperature, °C, degrees Celsius.

To recreate the effect of the cryoprotectant gel, phase transition of the skin water was not considered in the entire temperature range analyzed.

In order to simulate the suction effect of the applicator on the tissue to be cooled, the area of the treated biological tissue was divided into two parts: (1) the suctioned tissue, composed by the skin and fat inside the applicator; and (2) the non-suctioned tissue, composed by the skin and fat adjacent to the suctioned tissue. Due to the suction process, ischemia is caused in the suctioned tissue, which decreases the blood flow inside it. This decrease in blood flow reduces the biological heat produced by the suctioned tissue. Therefore, it is interesting to cause the greatest possible degree of ischemia to avoid the effect of the biological heat of suctioned tissue and achieve better cooling. Non-suctioned tissue, however, is a source of heat because of maximum blood flow. So, the contact surface between both tissue parts (suctioned and non-suctioned) has to be considered because the larger the contact surface, the higher the amount of heat transmitted to the suctioned tissue.

In a real-life situation, the ischemia caused by suction is incomplete and the biological heat affects the suctioned tissue in some extent. Two cases of "simulated suction" were considered in the simulation:

The first case (Case 1), assuming 100% ischemia, was simulated by removing blood perfusion of the suctioned skin and fat. However, for the fat and skin outside the receptacle of the applicator (non-suctioned surrounding tissue), biological heat in its natural state (100% of blood perfusion) was taken into account.

In the second case (Case 2), assuming partial ischemia, a model was developed to estimate a blood perfusion factor (BPF) in the suctioned tissue for each applicator, which was based on the following premises (Fig. 6):

a) BPF to be between 0 and 1, multiplying the frequency of blood perfusion (ω) of the biological tissue in its natural state. Without ischemia, the factor is 1, and there is natural biological heat; with 100% ischemia, the factor is 0 and biological heat is null.

b) BPF increases with the blood perfusion surface (surface of the suctioned tissue through which blood flows).

$$\text{Perfusion factor} = 1 - e^{-\left(k \times \frac{\text{Width of the applicator cavity}}{\text{Suction pressure} \times \text{Angle of cooling surfaces} \times \text{Depth}}\right)}$$

Figure 6. Equation for the ischemia factor.

e: constant with an approximate value of 2.71828; *k*: Constant to determine the perfusion factor for each applicator, obtained by applying the model to a reference value.

c) BPF decreases with the depth and the inclination angle of the lateral surfaces inside the applicator, and with suction pressure.

d) For high BPF values (low ischemia), changes in the design parameters do not significantly affect ischemia. On the other hand, for low BPF values (high ischemia), small design changes can significantly affect the resulting ischemia.

Data Analysis

Case 1: A 100% ischemia, and therefore, null biological heat in the suctioned tissue was considered. The variables analyzed for the Cooltech Define® and Cooltech® applicators were:

- *Cooling merit parameter:* The merit parameter obtained for the Cooltech® applicators was validated and used to assess the cooling capacity of the new Cooltech Define® applicators.
- *Cooling homogeneity:* It was determined from temperature distribution in the suctioned tissue at 35, 50 and 70 minutes of treatment.
- *Cooling dynamics:* The evolution of skin and fat average temperature inside the applicator was estimated during the 70 minutes of treatment.
- *Apoptosis:* The time required for fat to reach crystallization temperatures was estimated and set in this study at 10 ºC, temperature after which apoptosis in the adipose tissue could start.[2, 21–23] Based on the time elapsed, the fat percentage inside the applicators with a temperature under 10 ºC was also estimated.
- *Hypoesthesia:* The percentage of skin inside the applicator with a temperature under 7 ºC during the 70 minutes of treatment, and the time required for 50% of the skin inside the applicator to reach a temperature under 7 ºC, were estimated.

Case 2: Partial ischemia was considered and its effect on the above variables were analyzed.

- Evaluation of ischemia: For the Straight Cooltech® and Double Cooltech® applicators, the cooling effects were assessed as a function of the blood perfusion factor applied to the suctioned tissue. Blood perfusion factor was determined using efficacy clinical data of both applicators, and a mathematical model was used to determine blood perfusion factor for the rest of the applicators. More simulations were carried out.

Results

Cooling merit parameter: The cooling behavior of the applicators from both series is shown in Figure 7 and Figure 8; merit parameter values for the different Cooltech® and Cooltech Define® applicators are shown in Figure 9.

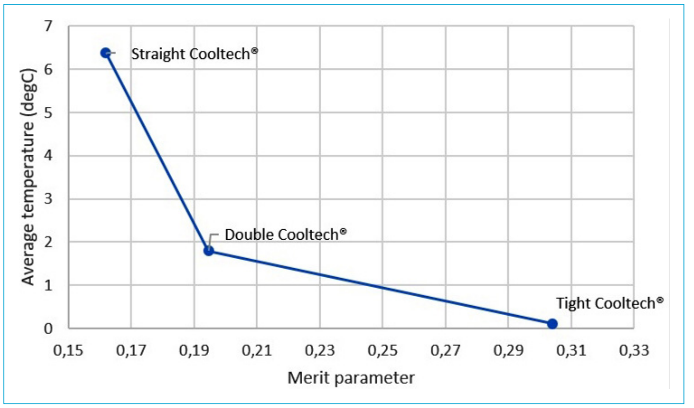

Figure 7. Fat average temperature at 70 minutes of treatment vs. the merit parameter for Cooltech® Straight, Double and Tight applicators.

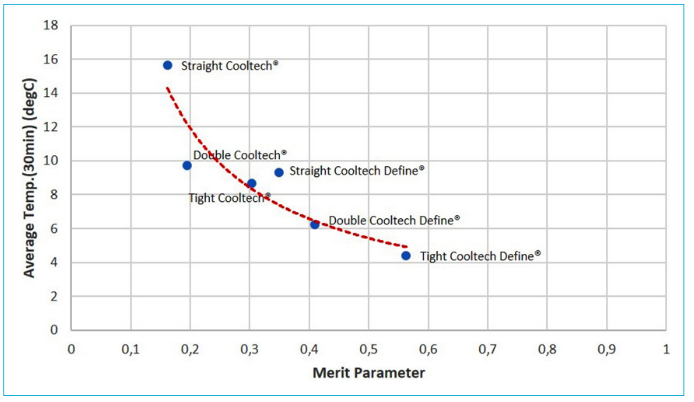

Figure 8. Fat average temperature at 30 min vs. the merit parameter for each Cooltech® and Cooltech Define® applicator. Abbreviations: Temp. temperature; min, minutes; degC, degree Celsius.

Cooling homogeneity: At 35 minutes, all Cooltech Define® applicators reached an internal temperature under 0 ºC on the entire tissue surface, while in the case of Cooltech® applicators, lateral surfaces cooled faster than top surfaces (Fig. 10).

Cooling dynamics: Figure 11 shows the results of the evolution of skin and fat average temperature during the 70

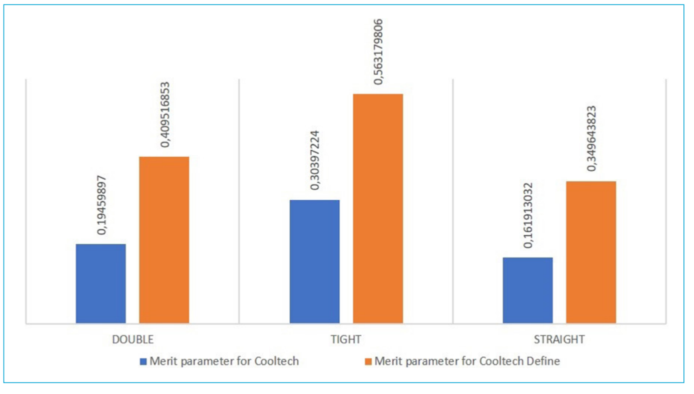

Figure 9. Comparative chart of the Cooltech® and Cooltech Define® applicators vs. their merit parameter.

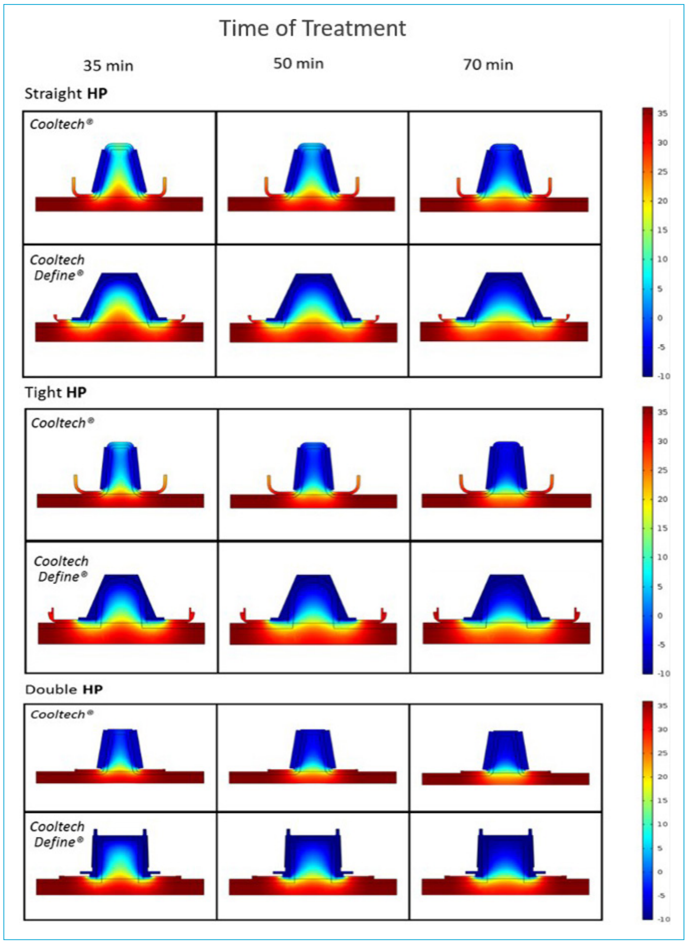

Figure 10. Cooling homogeneity: Comparison between the temporary evolution of temperature in the skin/fat-applicator system for each couple of equivalent Cooltech® and Cooltech Define® applicators: Straight (top), Tight (middle) and Double (bottom). Temperature decrease achieved.

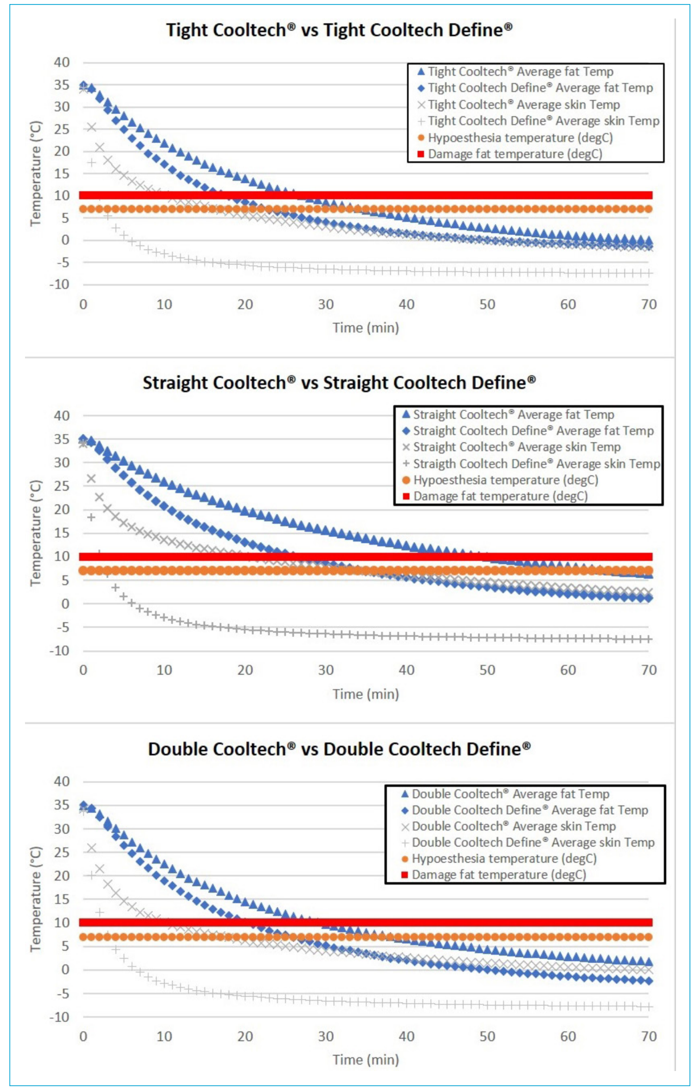

Figure 11. Temperature vs. Time chart: Cooltech® vs. Cooltech Define®.

minutes of treatment for each Straight, Tight and Double applicator model, both for the Cooltech® and Cooltech Define® series. Two horizontal lines have been included in the graphs, one indicating the temperature of apoptosis or crystallization of fat (10 ºC) and another one for the temperature of hypoesthesia of the skin (7 ºC).

Apoptosis: The time required for fat to reach apoptosis temperature, set at 10 ºC, is shown in Table 4. Values ranged from 17-25 minutes for the models of the Cooltech Define® series and from 26-48 minutes for those of the Cooltech® series (Table 4). The results of the evolution of fat percentage affected during the 70 minutes of treatment are shown in Figure 12. Cooltech Define® applicators showed an improvement of 15-20 percentage points compared to Cooltech® applicators.

Hypoesthesia: The time required for 50% of the skin inside the applicator to reach a temperature under 7 ºC (Fig. 13) was 3 minutes for Cooltech Define® series and a range of 8-26 minutes for the Cooltech® series (Table 5),

Ischemia: Figure 14 shows the dependence between the percentage of fat affected by cold in Cooltech® Straight and Double applicators at the end of a 70-minute treatment, and the blood perfusion factor applied to the tissue suctioned. A strong dependence between the affected fat

Table 4. Comparative table of mean times at which crystallization temperatures were reached

Series	Applicator Model	Time for fat to reach crystallizatio temperature (10.38 ºC)
Cooltech®	Straight	48
	Tight	26
	Double	28
Cooltech Define®	Straight	25
	Tight	17
	Double	19

ºC: degrees Celsius.

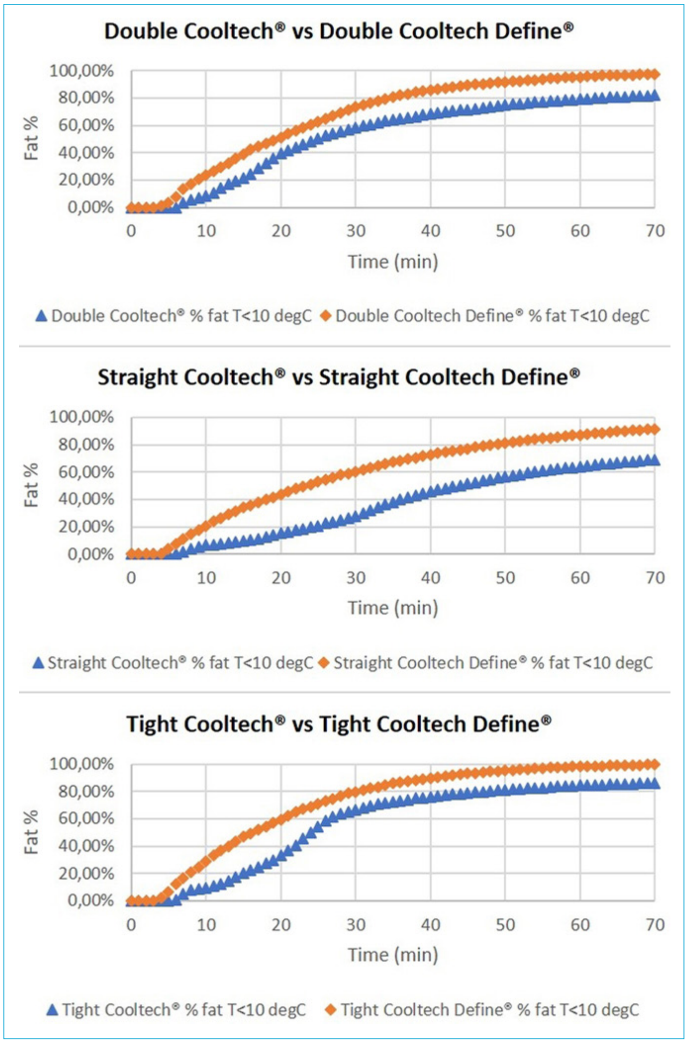

Figure 12. Fat % below 10 °C vs. time chart: Cooltech® vs. Cooltech Define®.

and blood perfusion was observed. Clinical studies carried out with Straight and Double Cooltech® applicators have shown an effectiveness in fat reduction for each applicator of about 20% and 25%, respectively [Dr. Serena's clinical study, not yet published]. These percentages corresponded to blood perfusion in the simulations for each applicator of 42% and 27%, respectively.

Figure 15 compares the result of the simulations for both applicators without blood perfusion (blood perfusion factor (BPF)=0) inside the suctioned tissue and with the BPF estimated. An isotherm curve of 10 ºC has been added to the graphics to compare the differences between both simulations. Table 6 shows the BPF for all the applicators of both series obtained from the model, as well as the results of the simulation for fat reduction percentage at the end of the treatment. Thus, from the simulations that included blood perfusion, the Cooltech® Straight, Double and Tight applicators showed fat reduction percentages of 21.05%, 25%, and 68.39%, respectively; while their Cooltech Define® counterparts showed fat reduction percentages of 49.13%, 77.47% and 73.97%, respectively.

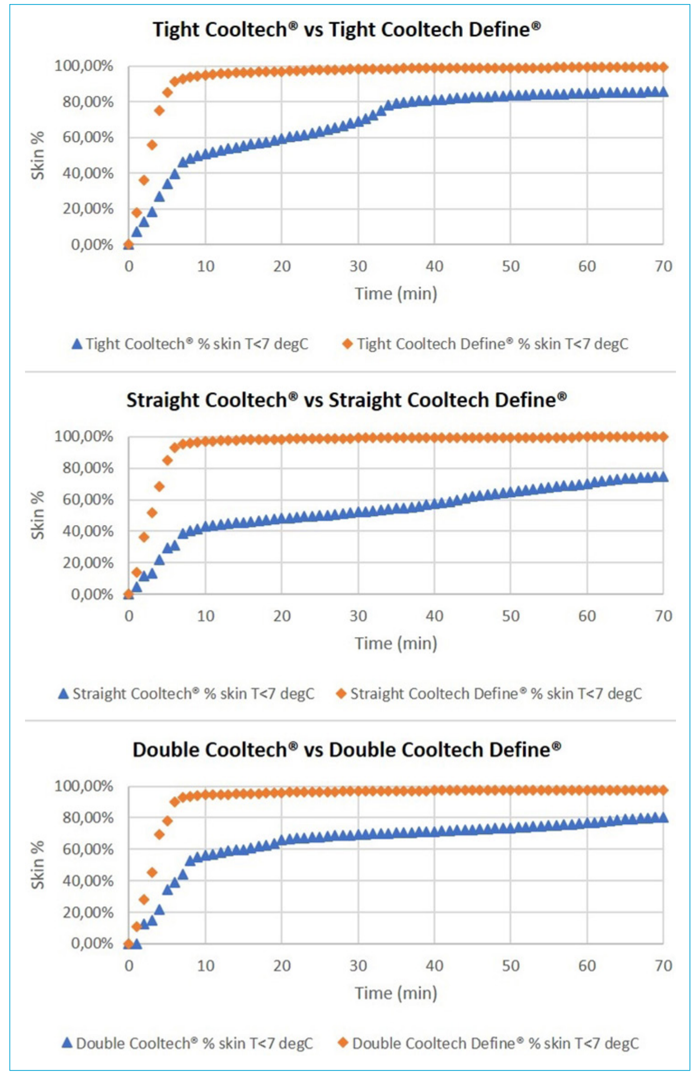

Figure 13. Skin % below 7 oC vs. time chart: Cooltech® vs. Cooltech Define®.

Table 5. Comparative table of mean times at which hypoesthesia temperatures were reached

Series	Applicator Model	Time required for 50% of the skin to reach a temperature below 7 ºC (min)
Cooltech®	Straight	26
	Tight	9
	Double	8
Cooltech Define®	Straight	3
	Tight	3
	Double	3

ºC: degrees Celsius; min: minutes.

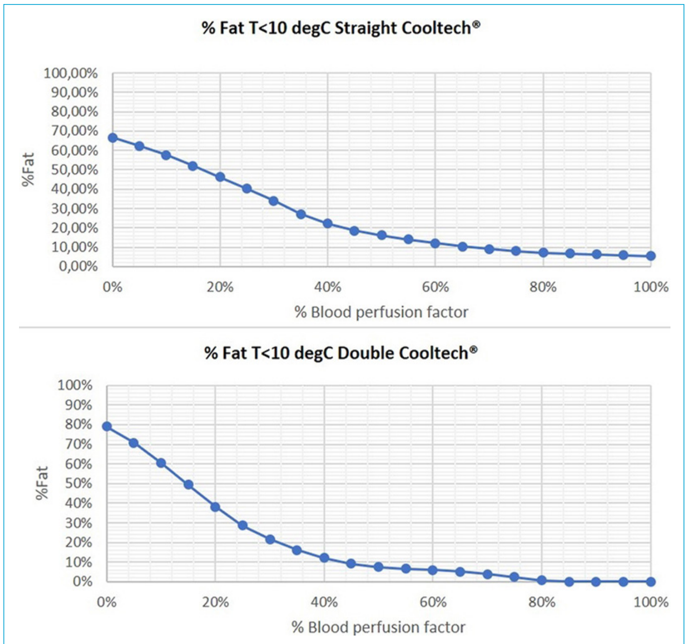

Figure 14. Fat percentage under 10 oC at 70 minutes of treatment based on the applied blood perfusion factor (expressed as a percentage) for Cooltech® Straight and Double applicators.

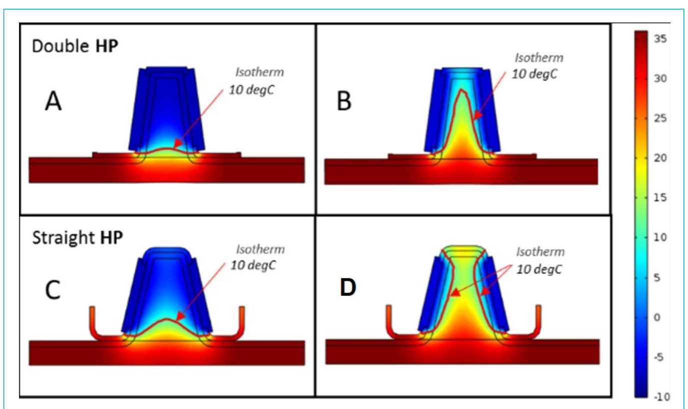

Figure 15. Cooltech® Double applicator without internal perfusion **(A)** and with 27% perfusion **(B)**; Cooltech® Straight applicator without internal perfusion **(C)** and with 55% perfusion **(D)**.

Table 6. Comparative table of the percentage of fat reduction based on the blood perfusion percentage applied in the simulation

Series	Applicator Model	% of Blood Perfusion	% of Fat Reduction at the End of Treatment
Cooltech®	Double	28	25
	Straight	42	21
	Tight	31	68
Cooltech Define®	Double	31	78
	Straight	49	49
	Tight	39	74

Discussion

The present study shows numerical simulations as an effective tool in the design of applicators for cryoadipolysis, allowing to evaluate the temperature inside cooled tissues with different real applicators and determining the behavior that new designs will have when compared to current models. In order to realize these simulations, a 3D heat transfer model has been used with all the integrated materials (tissues and applicator) and with temperature-dependent parameters.

Results obtained from the simulations conducted in this study showed that Cooltech Define® applicators had better cooling speed and homogeneity. The merit parameter of Cooltech® applicators proved to be appropriate as a starting point to design these new applicators since, as its value increased, so did the cooling of the suctioned tissue (Fig. 7). This behavior justified choosing that merit parameter and enabled to analyze the response of the new Cooltech Define® applicators during their design and compare the cooling capacity of both series of applicators in a simulation (Fig. 11). The merit parameter value obtained for the design of the new applicators was almost twice as high as that used to design the Cooltech® series applicators (Fig. 9).

At 35 min of treatment, the Cooltech Define® applicators managed to cool a larger percentage of internal tissue, and in a more homogeneous way, than their Cooltech® counterparts, being this difference, more apparent in Straight and Tight applicators. The temperature reached by Cooltech® applicators in the upper part was 10-15 ºC, whereas that of their Cooltech Define® counterparts reached 0 ºC in the same area. This improvement was due to the fact that the entire surface inside the Cooltech Define® applicators has cooling capacity, while the Cooltech® applicators only contain cooling plates on the sides of the inner cavity.

In both types of applicators, the temperature exponentially decreased with time (Fig. 11) and, as it could be expected, skin temperature dropped faster than fat temperature. Results clearly show that, at the end of the 70 min of treatment, fat cooling speed was faster, and the temperature reached was much lower with Cooltech Define® applicators, with a mean difference of 5 ºC between both series of applicators. Furthermore, when comparing the results of the time required for intracellular triglycerides to reach crystallization temperatures, it was observed that the applicators of the Cooltech Define® series showed a faster cooling speed than the Cooltech® series, confirming a larger and more homogeneous cooling capacity (-10 ºC) of the Cooltech Define® applicators vs. the Cooltech® applicators, which only reach a temperature of -8 ºC.

The evolution of the fat percentage crystallized with time was also different between both series of applicators (Figs. 13, 14). Cooltech Define® applicators showed an exponentially negative and homogeneous increase of affected fat over time, with a tendency to become stabilized at the end of treatment. In turn, Cooltech® applicators showed a first linear trend regarding fat cooling towards an exponentially negative behavior. Again, this behavior occurs because Cooltech Define® applicators cool fat in a homogeneous way thanks to an increased cooling surface. Furthermore, Cooltech Define® applicators reached a larger amount of fat affected than Cooltech® applicators at all times.

Regarding the time required for 50% of skin to reach hypoesthesia temperature, Cooltech Define® applicators achieved it at 3 minutes of treatment while Cooltech® applicators needed more time. These results indicate that Cooltech Define® applicators may provide patients with more comfort during treatment, since they would be able to numb the area faster than Cooltech® applicators.

Results from the second round of simulations revealed that including biological heat as a parameter in the simulations highly affected the results obtained. The results showed a strong relationship between the crystallized fat and blood perfusion or, in other words, the degree of ischemia applied in the simulation. With the Cooltech® Double applicator, the crystallized fat percentage without blood perfusion was virtually 80%, and after adjusting the ischemia value, this percentage dropped to 25%. When the ischemia model was applied to the new Cooltech Define® Double applicator, crystallized fat increased to 77%. The percentages of crystallized fat obtained for all three Cooltech Define® applicators (Double, Straight and Tight) were 77%, 49%, and 74%, respectively. These results suggest that the new Cooltech Define® applicators may offer fat reduction percentages of over 50%, which could be equivalent in effectiveness to surgical techniques.

Finally, to summarize, this study of numerical simulations shows how Cooltech Define® applicators reach a lower cooling temperature, presented a higher cooling speed, cooled the suctioned fat in a more homogeneous way, and reached hypoesthesia and a large percentage of crystallized fat faster than Cooltech® applicators at the end of treatment. Likewise, the inclusion of the degree of ischemia of the suctioned tissue in the simulation model was a highly relevant parameter to estimate the temperatures of adipose tissue inside the applicators. Clinical studies will be necessary to adjust blood perfusion for each type of applicator, both Cooltech® and Cooltech Define®, in order to determine fat reduction and the effectiveness of each series of applicators more accurately and be able to show the new Cooltech Define® applicators' improvements.

Disclosures

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References

1. Preciado J, Allison J. The effect of cold exposure on adipocytes: Examining a novel method for the noninvasive removal of fat. Cryobiology 2008;57:327.
2. Manstein D, Laubach H, Watanabe K, Farinelli W, Zurakowski D, Anderson RR. Selective cryolysis: A novel method of non-invasive fat removal. Lasers Surg Med 2008;40:595–604.
3. Avram MM, Harry RS. Cryolipolysis for subcutaneous fat layer reduction. Vol. 41, Lasers in Surgery and Medicine. 2009. p. 703–8.
4. Dierickx CC, Mazer JM, Sand M, Koenig S, Arigon V. Safety, tolerance, and patient satisfaction with noninvasive cryolipolysis. Dermatologic Surg 2013;39:1209–16.
5. Viera-Mármol G, García P, Villena J. Validation of Cooling and Freezing Dynamics of Cooltech® Using an Experimentally Adjusted Physical Model. SAS J Med. 2017.
6. Viera-Mármol G, Villena J, García P, Khrystova K, Colina M, Colina M. A Comparative Study of Cooltech® Handpieces for Cryoadipolysis Using Numerical Simulation. Probl Cryobiol Cryomedicine 2018;28:343–56.
7. Thermal Expansion Properties of Materials [Internet]. Vol. 10, Online. 1900 [cited 2018 Sep 14]. p. 225–32. Available from: https://www.professionalplastics.com/professionalplastics/ThermalPropertiesofPlasticMaterials.pdf
8. Pham QT. Food freezing and thawing calculations. Springer-Verlag New York; 2014. XV, 153.
9. COMSOL Multiphysics® Modeling Software [Internet]. [cited 2018 Sep 7]. Available from: https://www.comsol.es/
10. Alumina ceramic (94% alumina) [SubsTech] [Internet] [Internet]. Available from: http://www.substech.com/dokuwiki/doku.php?id=alumina_ceramic_94_alumina
11. Thermal Properties of Plastic Materials Material Formula Coefficient of thermal expansion x10 -6 K [Internet]. [cited 2018 Jun 4]. Available from: https://www.professionalplastics.com/professionalplastics/ThermalPropertiesofPlasticMaterials.pdf
12. Raulin C, Karsai S. Laser and IPL technology in dermatology and aesthetic medicine. Laser and IPL Technology in Dermatology and Aesthetic Medicine. SPRINGER;2011.1-419 p.
13. Williams LR, Leggett RW. Reference values for resting blood flow to organs of man. Clin Phys Physiol Meas 1989;10:187–217.
14. Raulin C, Karsai S, editors. Laser and IPL Technology in Dermatology and Aesthetic Medicine: Syrus Karsai: 9783642034374.

Berlin: Springer; 2011. 419 p.
15. Pinto H. Lipocryolysis: Cooling Speed Affects Adipocyte Survival. J Surg. 2015;3(1):11.
16. Garibyan L, Cornelissen L, Sipprell W, Pruessner J, Elmariah S, Luo T, et al. Transient Alterations of Cutaneous Sensory Nerve Function by Noninvasive Cryolipolysis. J Invest Dermatol. 2015;135:2623–31.
17. Tierney EP, Hanke CW. The effect of cold-air anesthesia during fractionated carbon-dioxide laser treatment: Prospective study and review of the literature. J Am Acad Dermatol. 2012;67:436–45.
18. Tatsutani KN, Joye JD, Virmani R, Taylor MJ. In vitro evaluation of vascular endothelial and smooth muscle cell survival and apoptosis in response to hypothermia and freezing. Cryo Letters 2005;26:55–64.
19. Abramovits W, Graham GF, Har-Shai Y, Strumia R. Dermatological cryosurgery and cryotherapy. Abramovits W, Graham G, Har-Shai Y, Strumia R, editors. Dermatological Cryosurgery and Cryotherapy. London: Springer London; 2016. 1-758 p.
20. Wowk B. HOW Cryoprotectants Work. Cryonics. 2007;Third Quar: 7.
21. Pinto H, Ricart-Jane D, Pardina E. X-ray diffraction study confirms intra-adipocitary lipid crystallization after lipocryolysis stimulus. Cryo Letters 2013;34:619–23.
22. Friedman DP. Commentary on: The safety and efficacy of cryolipolysis: A systematic review of available literature. Vol. 35, Aesthetic Surgery Journal. Oxford University Press; 2015. p. 837–8.
23. Zelickson B, Egbert BM, Preciado J, Allison J, Springer K, Rhoades RW, et al. Cryolipolysis for Noninvasive Fat Cell Destruction. Dermatologic Surg 2009;35:1462–70.