METHOD AND APPARATUS FOR HEATING BIOLOGICAL TISSUE

Abstract: Exemplary embodiments of apparatus and method for tissue heating using a plurality of hollow needles to deliver a heated fluid into the tissue can be provided. For example, a volume and/or temperature of the fluid can be controlled to heat the tissue to a particular temperature or to within a predetermined temperature range. The method and apparatus can be used for such procedures as hair removal or tumor treatment. A portion of the delivered heated fluid can optionally be aspirated from the tissue. The exemplary method and apparatus can also be used for fat removal, where heated fatty tissue can be thermally damaged and re-absorbed by the body, and/or aspirated through the hollow needles.
METHOD AND APPARATUS FOR HEATING BIOLOGICAL TISSUE

CROSS REFERENCE TO RELATED APPLICATION

The present application claims priority from U.S. Provisional Patent Application Serial No. 61/041,592 filed April 1, 2008, the disclosure of which is incorporated herein by reference in its entirety.

FIELD OF THE INVENTION

The present disclosure relates to exemplary embodiments of method and apparatus for heating a biological tissue using a plurality of needles to inject a heated fluid into a portion of the tissue. Such exemplary method and apparatus can also be used for a disruption of a fatty tissue, where a portion of the heated fluid and/or the heated fatty tissue can optionally be aspirated through the needles.

BACKGROUND INFORMATION

Heating of biological tissue can be used for a variety of purposes that may be therapeutic and/or aesthetic in nature. For example, controlled heating of certain tissue volumes can be used to cause effects such as hair removal, treatment of acne or venous lesions, fat reduction, treatment of certain tumors, etc. Such heating can be performed non-invasively, e.g., by directing energy from an external source into the tissue region to be heated. A variety of procedures can be used to selectively heat particular regions of tissue.

For example, various types of electromagnetic radiation can be directed into tissue to heat it. Such electromagnetic radiation can include, for example, optical energy such as laser light or intense pulsed light. Several techniques can be used to heat a region of tissue below the tissue surface using an external radiation source. For example, optical energy can be focused to a particular region below the tissue surface. A higher concentration of the radiation intensity in the focus region can provide heating of the region with relatively little heating of overlying tissue. Such focusing techniques are described, e.g., in U.S. Patent No. 6,997,923.
Chroraophores can also be used to facilitate localized tissue heating utilizing optical radiation. Such chromophores can selectively absorb certain wavelengths of optical energy to provide heating as compared with regions of tissue that have fewer or no such chromophores. Chromophores may occur naturally in the tissue, such as melanin or other pigments, or they may be introduced into regions of tissue to be heated.

Radio frequency ("RF") energy can also be directed into tissue to heat certain regions thereof. For example, the commercial Thermage procedure can direct RF energy into certain regions of tissue below the skin surface to achieve various effects. Ultrasound energy can also be directed into tissue to cause localized heating thereof.

Mechanical/acoustic ultrasound energy can also be focused to facilitate localized heating of particular target regions. Such focused ultrasound techniques are described, e.g., in U.S. Patent No. 6,1 13,559.

Surface cooling of tissue can also be used with a variety of the conventional heating techniques described herein. Surface cooling can help to reduce or avoid undesirable heating of surface portions of tissue when energy is directed into the tissue from an external source to heat target regions within the tissue. Such surface cooling can be achieved, e.g., using a cryospray, surface contact with a cooled object, or other conventional cooling procedures.

It may be difficult or impossible to heat certain precise target regions of tissue using the non-invasive heating techniques described above. In general, energy from an external source can pass through tissue overlying the target region, leading to some heating thereof. Tissue can also scatter various types of energy, which can reduce the precision of a localized application or focusing of energy. Target regions that lie deeper within the tissue can be even more difficult to selectively heat because of the greater amount of overlying tissue that can absorb and/or scatter the directed energy.

Excess fatty tissue can contribute to various health problems such as hypertension, heart disease, osteoarthritis, and other conditions. The presence of fatty tissue in various regions of the body may also be considered to be aesthetically undesirable. Reduction in the amount of fatty tissue present in various parts of the body, for both health and aesthetic reasons, is becoming more common. Various procedures, both invasive and non-invasive, can be used to remove fatty tissue directly or to facilitate its resorption by the body.
Fatty tissue can include both subcutaneous fat and adipocytes (fat cells). Subcutaneous fat can refer to fatty tissue lying just below the dermis. Various thicknesses of such fatty tissue may be present in different parts of the body. For example, large amounts of fatty tissue can often be found in the thighs, abdomen, and upper arms. In contrast, the facial region often may have a thinner layer of fatty tissue.

Liposuction is a known invasive procedure for surgically removing fatty tissue from selected portions of a patient's body. Liposuction may be used, for example, to contour selected body parts such as the abdomen, buttocks, hips, thighs, etc. where larger deposits of fatty tissue may be present. Liposuction can also be referred to as, for example, suctionspectum, lipolysis, or body contour surgery.

Conventional liposuction can be performed by inserting a hand-held tubular instrument 100 (e.g., a cannula) through an incision 120 in the surface of skin tissue 110, as shown in FIG. 1. The cannula 100 may typically have the form of a tube with a hollow central core that includes an aspirator tip 130 at a distal end. The cannula 100 can be positioned such that the tip is located within or adjacent to a portion of fatty tissue 140 to be removed. Fatty tissue 140 can then be aspirated through openings along the sides and/or tip 130 of the cannula 100, e.g., using vacuum from a syringe or pump. The aspirated fatty tissue 140 can be removed from the body through the cannula 100, and optionally deposited in a container provided in-line with the cannula and the vacuum source or otherwise disposed of.

During this exemplary procedure, the cannula 100 may be moved to a different position 150 such that the tip 130 can aspirate a larger volume of the fatty tissue 140 as it passes through the target region. Such movement may be lateral, as shown in FIG. 1, or along the length of the cannula axis (e.g., the cannula 100 can be further inserted or partially withdrawn from the skin tissue 110), or a combination of both types of motion can be performed. For example, liposuction procedures can often include a significant degree of such movement of the cannula 100 through the target region(s). This movement can help to mechanically break up the fatty tissue 140 to be removed, and facilitate its aspiration. Thus, liposuction procedures can be mechanically disruptive to tissue, even when a smaller cannula is used.

Accordingly, conventional liposuction techniques may often be accompanied by significant disruption of tissue structures within and adjacent to the fatty tissue being...
removed. For example, neighboring tissue surrounding the fat being removed, such as blood vessels and connective tissue, can be significantly damaged and/or partially removed along with the fatty tissue. Dangerous or undesirable side effects of conventional liposuction procedures can include, for example, disruption or severing of blood vessels, internal bleeding, pain, bruising, infection, and long recovery times.

Modifications to basic liposuction techniques and apparatus have been provided to make liposuction procedures safer, easier to perform, less painful, and/or more effective. For example, liposuction procedures may include an injection of an amount of fluid into the target region of tissue containing the fat to be removed. Such fluid can contain lidocaine as a local anesthetic, Epinephrine to locally contract blood vessels and reduce bleeding, and/or a saline solution which can help to loosen the fatty tissue and aid in its aspiration through the cannula. The amount of fluid injected into the fatty tissue to be removed may be determined based on such factors as the particular technique being performed, the location and size of the target region being treated, etc.

Disruption and/or removal of fatty tissue can also be achieved by certain non-invasive techniques. For example, physical exercise can help to reduce the amount of fatty tissue in the body. Nutritional supplements have also been formulated which, when ingested, can boost the body's metabolism and lead to increased 'burning' and reduction of fatty tissue. Certain compounds applied topically to the skin surface can also be absorbed and may lead to a reduction in the amount of subcutaneous fatty tissue over time. However, such non-invasive techniques can have limited effectiveness and/or may require long times, e.g., on the order of weeks or months, to produce noticeable results. Targeting of specific regions of fatty tissue may also not be easily achieved or even possible using these techniques.

Other non-invasive techniques which can be used for reduction of fatty tissue may include a heating of such tissue to disrupt tissue structures and promote resorption of the fatty tissue by the body. Heating of targeted fatty tissue can be performed, for example, by applying energy through the overlying skin. Forms of energy that can be used to thermally disrupt fatty tissue include, e.g., ultrasound energy, which can be applied in the form of focused ultrasound waves. Electromagnetic energy, such as radiofrequency ("RF") energy or laser energy, can also be used to heat fatty tissue. Focusing of the applied energy into the target region of tissue and/or cooling of the skin surface above the
target region can be performed, for example, to alleviate or prevent thermal damage to the dermis when the subcutaneous tissue is heated. Because such energy applied from outside the body still passes through the dermis, a localized heating of fatty tissue together with a protection of dermal tissue from thermal damage can be difficult to achieve.

In view of the shortcomings of the above described procedures for tissue heating and fat removal, it may be desirable to provide exemplary embodiments of method and apparatus that can combine safe and effective heating of target regions of tissue and/or disruption of fatty tissue while minimizing unwanted damage to surrounding tissue.

SUMMARY OF EXEMPLARY EMBODIMENTS

Exemplary embodiments of the present disclosure provide method and apparatus for heating tissue that can be minimally invasive, and that can provide localized heating of tissue while largely avoiding undesirable side effects such as excessive heating of a surrounding tissue. For example, a heated fluid can be dispersed directly within a target region of tissue using, e.g., a plurality of hollow needles inserted into the skin. The hollow needles can be provided as a needle array that is affixed to or coupled to a base or substrate. The heated fluid can include a saline solution, lidocaine, a detergent, an anti-inflammatory, and/or other components that can disrupt the targeted tissue and/or provide beneficial effects therein.

An exemplary diameter of the hollow needles can be, e.g., less than about 1000 μm, less than about 800 μm, less than about 500 μm, or even less than about 200 μm. An exemplary distance between adjacent hollow needles can be less than about 10 mm, less than about 8 mm, or less than about 5 mm. A length of the needles protruding below a lower surface of the base can be at least about 1 mm, or between about 1 mm and about 5 mm, or greater than about 5 mm, depending on the location of the tissue region to be heated. The needles can have the same length or some of the needles can have different lengths. An adjustable plate can be coupled to the base, such that the needles protrude through holes in the plate, and lengths of the needles protruding from the lower surface of the plate can be adjusted by adjusting the distance between the plate and the substrate. The exemplary array of needles can include, e.g., at least 10 needles, or at least 30 needles, or even at least 50 needles.
The local temperature of the heated tissue can be monitored, for example, using a temperature sensor provided in proximity to the tissue being heated. Such temperature can be used to control an amount and/or temperature of heated fluid provided to the target region to achieve and/or maintain a particular temperature or temperature range of the heated tissue.

Exemplary embodiments of the present disclosure can facilitate, for example, a disruption and/or thermal damage to hair follicles to facilitate hair removal, or to a tumor. Fatty tissue can also be heated to promote resorption of the targeted fatty tissue by the body. In further exemplary embodiments, a portion of the heated fluid and/or heated fatty tissue can be aspirated through the hollow needles using a source of low pressure, e.g., a vacuum pump. The exemplary aspiration can be performed following a suitable or predetermined time interval after introduction of the heated fluid into the target tissue. The heated fluid can facilitate the subsequent aspiration process, for example, by reducing the viscosity of the fatty tissue and/or by disrupting the fatty tissue (e.g., emulsifying or breaking down portions of the targeted tissue structure) as a result of reactions between the fatty tissue and certain components of the fluid.

These and other objects, features and advantages of the present disclosure will become apparent upon reading the following detailed description of the exemplary embodiments of the present disclosure, when taken in conjunction with the appended claims.

**BRIEF DESCRIPTION OF THE DRAWINGS**

Further objects, features and advantages of the present disclosure will become apparent from the following detailed description taken in conjunction with the accompanying figures showing illustrative embodiments, results and/or features of the exemplary embodiments of the present disclosure, in which

- Fig. 1 is a schematic illustration of a conventional liposuction procedure and a conventional apparatus to perform such conventional procedure,
- Fig. 2 is a schematic illustration of an apparatus for disrupting fatty tissue according to a first exemplary embodiment of the present disclosure,
Fig 3 is a schematic illustration of a distal portion of a hollow needle which can be used with the exemplary apparatus as shown in Fig 2, as well as with other exemplary embodiments of the apparatus as described and shown herein,

Fig 4 is a schematic illustration of an apparatus that can be used for heating tissue according to another exemplary embodiment of the present disclosure,

Fig 5A is a schematic plan view of one exemplary embodiment of an array of hollow needles that may be used with the exemplary embodiments of the apparatus according to the present disclosure,

Fig 5B is a schematic plan view of another exemplary embodiment of the array of hollow needles that may be used with the exemplary embodiments of the apparatus according to the present disclosure,

Fig 6 is a schematic illustration of a second exemplary embodiment of the apparatus that can be used to heat tumorous tissue according to the present disclosure, and

Fig 7 is a schematic illustration of a third further exemplary embodiment of the apparatus that can be used to facilitate hair removal according to the present disclosure

Throughout the drawings, the same reference numerals and characters, unless otherwise stated, are used to denote like features, elements, components, or portions of the illustrated embodiments. Moreover, while the present disclosure will now be described in detail with reference to the figures, it is done so in connection with the illustrative embodiments and is not limited by the particular embodiments illustrated in the figures.

DETAILED DESCRIPTION OF EXEMPLARY EMBODIMENTS

Exemplary embodiments of the present disclosure provide methods and apparati for reduction of fatty tissue by disruption and/or removal thereof. A schematic diagram of a first exemplary embodiment of an apparatus 200 for reduction of fatty tissue according the present disclosure is shown in FIG 2. For example, the exemplary apparatus 200 can include a plurality of hollow needles 220 that can be affixed or coupled to a base 210. A reservoir 230 configured or structured to hold a heated fluid can be provided in communication with the hollow needles 220 via a conduit 240. An optional heating arrangement 250 may be coupled to the reservoir 230. A valve arrangement 295 and/or a pump 260, or another flow control arrangement, can also be provided in communication with the conduit 240 to control the amount and/or rate of flow of the fluid therethrough. In
certain exemplary embodiments, an optional spacer plate 270 and posts 273 may be provided to adjust a distance at which the needles 220 extend from the lower surface of the apparatus 200. A vibrating arrangement 275 can also be provided to facilitate the insertion of the needles 220 into the tissue 283. A temperature sensor 290 can optionally be provided to measure and/or monitor the temperature of the heated fatty tissue 285. A vacuum pump 297 may optionally be provided in communication with the conduit 240, e.g., through the valve arrangement 295 or a further valve arrangement, to facilitate the fatty tissue 285 to be aspirated through the needles 220.

Each needle 220 may be formed using or consist of a metal or alloy, e.g., a surgical steel or the like. Other materials that exhibit appropriate mechanical and/or thermal properties for structural strength, etc., can also be used to form the needles 220. Combinations of materials can also be used to form the needles 220 such as, e.g., a needle formed of a surgical steel coated with a thin layer of a polymer. The needles 220 can be formed using a material that does not have a high thermal conductivity, such as a composite material, a polymer or plastic, a crystalline material such as a semiconductor, etc. The hollow needles 220 can have a cross-sectional shape that is round, oval, or any other shape that provides structural rigidity and facilitates flow of a fluid through a central hollow portion.

The hollow needles 220 can be small enough in diameter to be inserted into the skin tissue 283 without causing significant tissue damage or pain to the subject, and large enough to facilitate a passage of fluid through the hollow central portion thereof. For example, the outside diameter of one or more of the needles 220 can be less than about 1000 µm, or less than about 800 µm in certain exemplary embodiments. The needles 220 having a diameter of less than about 500 µm, for example, about 300 µm in diameter, can also be used if they are sufficiently stiff for a reliable insertion into skin tissue. The needles 220 wider than about 1000 µm in diameter can also be used in accordance with certain exemplary embodiments of the present disclosure, and such larger needles 220 can be less preferable, e.g., because of a difficulty in forcing larger needles to penetrate the skin and/or an increased likelihood of pain and/or scarring. An inner diameter of each hollow needle 220 (e.g., a cross-sectional diameter of the hollow portion) can be made as large as possible while maintaining sufficient structural and mechanical strength of the needle 220 to facilitate the insertion and removal thereof from the skin tissue 283 without
breaking the needles 220. For example, a larger inner diameter of one or more of the needles 220 can facilitate an increased flow of fluid through the hollow needle 220 and/or provide an easier aspiration of tissue therethrough.

A distal end of the hollow needle 220 can be cut, abraded, molded, or otherwise shaped to form a sharp point or edge, such as the exemplary distal end 300 shown in Fig. 3. Such sharp edge or point can facilitate a penetration of the distal end 300 of the hollow needles 220 into and/or through the upper portion 280 of the skin tissue 283 (e.g., through the epidermal and dermal layers), such that a distal portion of the needles 220 can be positioned proximal to or within the subcutaneous layer of fatty tissue 285.

The distal ends 300 can optionally be formed using a material that is different than the material used to form the walls of the needle 220, which can further facilitate the insertion of the needles 220 into the skin tissue 283. For example, a portion of the needles 220 can be coated with a lubricant or low-friction material, such as Teflon® or the like, to further facilitate the passage of the needles 220 through the tissue 283.

In exemplary embodiments, one or more holes 310 or other apertures can be provided through the walls of the hollow needle 220 near the distal end 300, as shown in Fig. 3. These holes 310 can further facilitate a flow of fluid through the central hollow portion of the needle 220 and into the tissue surrounding the distal end 300.

The base 210 can be a plate, a substrate, a portion of a housing, or another structure that can be rigid, and which can be configured to hold the plurality of the needles 220 in a particular configuration. Some or all of the needles 220 can be substantially parallel to one another to facilitate their insertion and removal from the skin tissue 283.

The length of the needles 220 protruding beyond the base 210 that can penetrate into the skin tissue 283 can be selected based on a local depth of the fatty tissue layer 285 to be treated. The depth of the fatty tissue 285 can be about 3000 μm or greater in many regions of the body, although shallower or deeper distances can be used for different treatments. For example, the lengths of the needles 220 can be shorter for treatment of facial regions, and longer for treatment of deeper regions of fatty tissue 285 such as those located, e.g., in the upper arms, thighs, abdomen, etc.

In certain exemplary embodiments of the present disclosure, the hollow needles 220 can have different lengths. This can facilitate the needles 220 to extend to different depths within the fatty tissue 285 when they are inserted into the skin tissue 283.
as shown in Fig. 4. This variation in needle lengths can facilitate the fatty tissue present at a plurality of depths to be treated as described herein, based on a single insertion of the hollow needles 220.

In certain exemplary embodiments, the apparatus 200 can include a spacer plate 270 located between the base 210 and the surface of the skin tissue 283 over the area to be treated. The spacer plate 270 can be coupled to the base 210 by the posts 273, which can be provided with a screw-type mechanism. Another coupling arrangement can be provided between the spacer plate 270 and the base 210, e.g., that can be configured and/or structured to controllably vary a distance between the spacer plate 270 and the substrate 210. The needles 220 can be configured or structured to protrude through holes provided in the spacer plate 270. In this manner, the distance which the needles 220 extend below the surface of the spacer plate 270 can be varied by adjusting the distance between the substrate 210 and the spacer plate 270 using the posts 273. The spacer plate 270 can thus provide a selection and/or variation of the depth to which the needles 220 extend into the fatty tissue layer 285, for example, when the needles 220 are inserted into the skin tissue 283 until the spacer plate 270 contacts the surface of the skin tissue 283. The spacer plate 270 can also provide mechanical stability to the array of hollow needles 220.

The lower surface of the base 210 and/or the spacer plate 270, if provided, may have a substantially planar shape or they may be contoured to follow a surface contour of the region of tissue being treated. For example, the bottom surface of the base 210 and/or the spacer plate 270 can be planar, or convex, or concave with particular curvatures.

In certain exemplary embodiments, the needles 220, the base 210 and/or the spacer plate 270, if provided, can be cooled prior to inserting the needles 220 into the tissue 283. The cooling can be provided using any suitable technique (for example, by conduction via embedded conduits containing a circulating coolant or the like, use of a cryospray, or a Peltier device). The cooled components of the exemplary apparatus 200 can assist to reduce or eliminate perceived pain when the needles 220 penetrate the skin tissue 283. The surface portion 280 of the skin tissue 283 can also be pre-cooled directly prior to the insertion of the needles 220, e.g., using conventional cooling techniques, e.g., convective or conductive techniques such as applying a cryospray or contacting the upper surface with a cooled object.
In a further exemplary embodiment, a vibrating arrangement 275 can be mechanically coupled to the base/substrate 210 and/or the needles 220. The vibrating arrangement 275 can include, for example, a piezoelectric transducer, a small motor with an eccentric weight fixed to a shaft thereof, or the like. The vibrations induced in the needles 220 by the vibrating arrangement 275 can facilitate the piercing of the surface of the tissue 283 by the needle tips and the subsequent insertion of the needles 220 into the dermal tissue 280.

The vibrating arrangement 275 can have an amplitude of the vibration that can be between about 50 µm and about 500 µm, or optionally between about 100 µm and about 200 µm. The frequency of the induced vibrations can be between about 10 Hz and about 10 kHz, and/or between about 500 Hz and about 2 kHz, and even more preferably about 1 kHz. For example, vibration parameters can be selected based on the size, average spacing, and material of the needles 220, the number of needles in the apparatus 200, and the tissue being treated. The vibrating arrangement 275 can further include circuitry configured to adjust the amplitude and/or frequency of the vibrations.

The needles 220 of the exemplary apparatus 200 shown in Fig. 2 can be provided in a two-dimensional arrangement, where the needles 220 can be substantially parallel to each other and substantially perpendicular to the surface of the skin tissue 283 being treated. For example, the needles 220 can be arranged through the base/substrate 210 in an exemplary regular or near-regular square pattern 500 as shown in Fig. 5A, or in an exemplary triangular pattern 510 as shown in Fig. 5B. Other exemplary patterns or arrangements of the needles 220 can be used, including non-uniform or irregular patterns.

The relative positions and spacing of the needles 220 can be determined based on the desired treatment to be performed. The exemplary spacing (e.g., lateral distance) between adjacent needles 220 can be less than about 10 mm, or less than about 8 mm. Optionally, the spacing between the adjacent needles 220 in the array can be less than about 5 mm, and/or even less than about 2 mm. The spacing between the needles 220 need not be uniform, and can be smaller in areas where a relatively greater amount of tissue heating and/or fat disruption or removal is desired. For example, a closer spacing of the needles 220 can facilitate greater amount of volumetric tissue heating when a particular amount of heating fluid is provided through each needle. Alternatively, a wider spacing of the needles 220 can facilitate the treatment of a larger region of tissue 283.
Various numbers of the needles 220 can be provided in the exemplary apparatus 200. For example, the apparatus 200 can include at least about 10 needles 220, at least about 30 needles 220, or at least about 50 needles 220. Exemplary arrays having a larger number of the needles 220 can be used, e.g., to treat a larger volume of the tissue 283 with a single insertion of the needle array into the skin. A larger region of the tissue 283 can also be treated by a sequential insertion of the needles 220 in proximal locations. The number of the needles 220 provided in the apparatus 200 can be selected based on various factors such as, e.g., ease of manufacture, a desired needle spacing, the size of the region to be treated, etc.

The apparatus 200 can facilitate a controllable delivery of a heated fluid from the reservoir 230 through the hollow needles 220 via the conduit 240 using the pump 260. The fluid can be directed into predetermined regions of the fatty tissue 285 near the distal ends of the needles 220. For example, specific portions of the fatty tissue 285 can be heated directly by the heated fluid while avoiding an undesirable amount of thermal damage to the dermal layer 280 located above the fatty tissue 285. By using an array of such hollow needles 220, a large region of the fatty tissue 285 can be heated by the hot fluid following a single insertion of the array of the hollow needles 220 into the skin tissue 283.

The exemplary apparatus 200 can be used, for example, to heat the fatty tissue 285 to a temperature that is high enough to cause thermal damage or disruption without causing excessive necrosis. Such target temperature of the heated fatty tissue 285 can be, for example, between about 42 °C and about 48 °C. Prolonged heating of fatty tissue to temperatures greater than about 48 °C can lead to undesirable necrosis, fibrosis, and/or formation of scar tissue.

The temperature of the heated fluid in the reservoir 230 can be controlled by the heater 250, which may include control circuitry that allows this temperature to be set and maintained at a particular value. The amount and/or flow rate of heated fluid delivered to a region of the fatty tissue 285 through the hollow needles 220 can be controlled by the pump 260 and/or the valve arrangement 295.

The amount and temperature of the heated fluid provided to heat the fatty tissue 285 to a particular temperature can be estimated using conventional energy calculations. For example, a volume of heated fluid provided to a portion of the fatty
tissue 285 can be between about 30% and 150% of the volume of the fatty tissue 285 to be heated. Other local amounts of heated fluid can be provided to the tissue 285, e.g., based on characteristics of the fluid and of the fatty tissue 285. The local volume of the fatty tissue 285 which can be heated to a particular temperature or temperature range by the fluid can be estimated based on the spacing of the hollow needles 220. This volume can be somewhat larger if the needles 220 are of different lengths, as described herein and shown in Fig. 4.

For example, the heat capacity of a fluid which includes mostly water is about twice the heat capacity of fat. Thus, a mixture containing equal volumes of water and fat can have a resulting temperature that is between the temperatures of each of the unmixed materials, and based on an assumption of good local mixing it may be about 2/3 closer to the temperature of the heated water-based fluid. For example, adding a volume of water at 49 °C to a volume of fat at 37 °C (which is approximately normal body temperature) can result in an average local temperature of about 45 °C (which is about 2/3 of the difference between 37 °C and 49 °C). This temperature is only approximate, as there may be only partial local mixing of the two substances and will some local temperature gradients within the mixture that can gradually even out. Further, the excess heat provided by the heated liquid can gradually diffuse and dissipate into surrounding tissue. Accordingly, the fluid in the reservoir 230 can be preferably greater than about 45 °C, or greater than about 50 °C, or optionally greater than about 55 °C, to locally heat the fatty tissue 285 to a suitable average temperature, e.g., between about 42 °C and about 48 °C without requiring a relatively large volume of heated fluid relative to the tissue volume.

The exemplary apparatus 200 can further include one or more temperature sensors 290. The temperature sensor 290 can be provided in a needle shape, with a sensing portion located near or at a distal end thereof, e.g., such that the sensing portion is proximate to the distal portion of one or more hollow needles 220. The sensor 290 can be configured to detect a local temperature in the fatty tissue 285 being treated, and optionally communicate with a display or other external arrangement to indicate the local temperature in the fatty tissue 285. The sensor 290 can also communicate with control circuitry associated with, e.g., the heater 250 and/or the pump 260 in a feedback arrangement or the like to vary the temperature of the fluid in the reservoir 230, which can facilitate heating of the tissue 285 to a more precise treatment temperature.

-- 13 --
The heated fluid can be water-based, such as a saline solution or other fluid that is preferably biologically compatible with the tissue being treated (e.g., a fluid that does not create an adverse reaction or effect when injected into a tissue). For example, the heated fluid can be similar to a fluid that can be used in conventional liposuction procedures. The fluid can optionally include one or more of an analgesic agent such as lidocaine, a detergent composition, an anti-inflammatory substance, a dispersing or emulsifying agent, etc. Various fluid components that can be used to facilitate disruption or damage of fatty tissue are described, for example, in U.S. Patent Publication No. 2006/0154906. The components of the heated fluid can be selected to provide effective disruption of the fatty tissue 285, reduce pain or chance of infection, etc. Application of such fluids using the exemplary apparatus 200 described herein can improve their efficacy by providing them in a heated state that is well-dispersed within the target fatty tissue 285 using the array of the needles 220.

In a further exemplary embodiments, the apparatus 200 can include a valve 295 arrangement provided in communication with the conduit 240 and a vacuum pump 297. In additional exemplary embodiments of the present disclosure, a further conduit can be provided that connect the vacuum pump 297 and the needles 220, optionally via a further valve arrangement. After a heated fluid is provided to the fatty tissue 285 as described herein, a portion of the heated fatty tissue 285 can be aspirated and removed through the hollow needles 220 by activating the vacuum pump 297 and/or the valve arrangement 295. For example, in certain exemplary embodiments, the valve arrangement 295 can be adjusted to block the supply of heated fluid from the reservoir 230 after the heated fluid has been injected into the tissue 285, and to open a path between the conduit 240 and the vacuum pump 297. The vacuum pump 297 can include circuitry configured to control an amount of fatty tissue is aspirated and the rate of aspiration. Heated fluid mixed with the fatty tissue 285 may also be aspirated. The heated fluid, when applied to and mixed with regions of the fatty tissue 285 as described herein, can thermally damage and/or disrupt the structure of the fatty tissue 285 and facilitate aspiration of the fatty tissue 285 and/or heated fluid through the needles 220.

The aspiration can be performed after an appropriate time interval following the application of the heated fluid to the fatty tissue 285. This time interval can be between about several seconds and several minutes or more, and it may be selected to allow heat
from the heated fluid to diffuse sufficiently through the fatty tissue 285 and/or to facilitate certain components of the fluid to interact appropriately with the fatty tissue 285. A particular time interval between introducing the heated fluid and aspiration of the mixture of heated fluid and fatty tissue 285 can be selected based on the temperature and composition of the fluid, the size and spacing of the needles 220, etc. This exemplary procedure can optionally be repeated, e.g., at a different depth (or depths) without removing the needles 220 from the tissue 283 by adjusting the spacer plate 270 so the distal ends of the needles 220 are located at a different depth within the fatty tissue 285. In this manner, a larger volume of the fatty tissue 285 can be heated, and/or disrupted and optionally aspirated based on a single insertion of the needles 220 into the tissue 283.

In a further exemplary embodiment of the present disclosure, the exemplary apparatus 200 can be used for treatment of a tumor-bearing tissue. For example, tumors may often have a reduced blood supply and can be particularly sensitive to heating. Accordingly, such undesirable tumors can be damaged or destroyed by heating the tumors to a temperature above normal body temperature for a particular time. Treating tumors by heating them is described, e.g., in U.S. Patent No. 4,140,130.

An exemplary apparatus 600 for treating tumors in accordance with exemplary embodiments of the present disclosure is shown in Fig. 6. The apparatus 600 can include a plurality of the hollow needles 220 that can be affixed or coupled to the base 210, similar to the exemplary apparatus 200 shown in Fig. 2. The reservoir 230 configured or structured to hold a heated fluid can be provided in communication with the hollow needles 220 via the conduit 240, and the heating arrangement 250 can be thermally coupled to the reservoir 230. The valve arrangement 295 and/or the pump 260 can also be provided in communication with the conduit 240 to control an amount and rate of flow of the fluid therethrough.

The length of the needles 220 can be configured or provided such that a distal portion of the needles 220 is positioned within and/or proximal to a region of tumor-bearing tissue 610 when the needles are inserted into the tissue 605. In certain exemplary embodiments, the optional spacer plate 270 and the posts 273, such as those shown in Fig. 2, can also be provided to adjust a distance at which the needles 220 extend into the tissue 605. A temperature sensor 290, similar to that shown in Fig. 2, can also be provided to measure and/or monitor the temperature of the heated tumor tissue 610.
The exemplary apparatus 600 can be operated in a procedure similar to that described herein for the exemplary apparatus 200 shown in Fig. 2. For example, tumor-bearing tissue 610 can be treated by heating it to a temperature between about 42 °C and about 50 °C, for a period of time that can be greater than about 15 minutes, e.g., for about 30 minutes or more. Temperatures and/or times that lie outside of these exemplary ranges can also be used for certain treatments. As described herein, the elevated temperatures can be maintained for extended periods of time by, for example, periodically injecting particular volumes of heated fluid through the hollow needles 220 and into the target region of tissue. The timing and volume of such applications of the heated fluid, as well as the temperature thereof, can be selected and/or controlled based on a local measured temperature using the temperature sensor 290 or any other indicator of the tissue temperature.

In further exemplary embodiments, a vacuum or low pressure arrangement, similar to the vacuum pump 297 can also be provided in communication with the needles 220 as shown, for example, in Fig. 2. For example, the vacuum pump 297 can be used to aspirate heated fluid that has been injected into the target region of tissue (e.g., the tumor-bearing tissue 610) after this tissue has been heated and the heated fluid has cooled off. This exemplary aspiration procedure can remove some or all of the heated fluid, facilitating additional heated fluid to be provided to the target region while avoiding an excessive buildup of the fluid in or near the target region.

Still further exemplary embodiments of the present disclosure can be used to assist in hair removal. Heating of hair sheaths and/or hair bulbs can damage the hair structure and lead to temporary or permanent hair removal. Conventional hair removal systems may include a laser or the like that is configured to selectively heat portions of the hair structure.

An exemplary apparatus 700 for hair removal in accordance with additional exemplary embodiments of the present disclosure is shown in Fig. 7. The exemplary apparatus 700 can include a plurality of the hollow needles 220 that can be affixed or coupled to the base 210, similar to the exemplary apparatus 200 shown in Fig. 2. The reservoir 230 configured or structured to hold a heated fluid can be provided in communication with the hollow needles 220 via the conduit 240, and the heating arrangement 250 can be thermally coupled to the reservoir 230. The valve arrangement
and/or the pump 260 can also be provided in communication with the conduit 240 to control an amount and rate of flow of the fluid therethrough. The base 210 can be formed as part of a housing or handpiece 710. In certain exemplary embodiments, the base 210 can be configured to be removably attached or coupled to the handpiece 710.

The length of the needles 220 can be configured such that a distal portion of the needles 220 is positioned at a depth that is proximal to hair bulbs 720, e.g., within and/or proximal to the dermal/fatty layer junction 730. In certain exemplary embodiments, the optional spacer plate 270 and the posts 273, such as those shown in Fig. 2, can also be provided to adjust a distance at which the needles 220 extend into the tissue 705. The temperature sensor 290 can also be provided to measure and/or monitor the temperature of the heated tissue proximal to the hair bulbs 720.

The exemplary apparatus 700 can be operated in a procedure similar to that described herein for the exemplary apparatus 200 shown in Fig. 2. For example, tissue proximal to the hair bulbs 720 may be briefly heated it to a temperature between about 50 °C and about 70 °C. Such heating may be transient, e.g., by providing a single injection of heated fluid having a relatively high temperature and a relatively small volume. For example, fluid having a temperature, e.g., between about 70 °C and about 90 °C and a volume between about, e.g., 0.1 ml and about 1 ml can be provided through each needle 220 and into the target region of tissue.

Such heating procedure can provide a rapid local heating of the tissue, followed by cooling as the thermal energy from the heated fluid dissipates into the surrounding tissue. Other fluid temperatures and/or volumes may also be used for certain treatments. The temperature and volume of the injected heated fluid can be selected and/or controlled, for example, based on a local measured temperature using the temperature sensor 290 or any other indicator of tissue temperature. Cooling of the skin surface above the target region can also be provided using conventional cooling techniques to reduce thermal heating and/or damage to tissue lying above the dermal/fatty layer junction.

In a further exemplary embodiment of the present invention, a method can be provided for localized heating of tissue such as, e.g., the fatty tissue 285 or tissue located within the dermis layer 280. A plurality of the hollow needles 220 can be inserted into tissue such that the distal portions of the needles 220 are located within or proximal to the tissue to be heated, e.g., as shown in Fig. 2. A heated fluid as described herein can be
provided from the reservoir 250 or the like through the hollow needles 220 and into the targeted tissue 285. Heat and/or components in the fluid can disrupt or thermally damage the fatty tissue 285, and optionally promote its resorption by the body. Such exemplary technique can facilitate a precise targeting of particular regions of the fatty tissue 285 to be heated. For example, in contrast to many conventional non-invasive tissue heating techniques, the exemplary techniques of the present disclosure can provide thermal energy directly to the target tissue to be heated without the energy passing directly through tissue portions located above the target region. Although the needles 220 can become warm and provide some heating to tissue away from the target region, this heating can be very small compared to that resulting from the hot fluid being provided directly into the target region itself. The needles 220 can be formed using a thermally non-conductive material to reduce heating of tissue adjacent or proximal to the non-distal portions of the needles 220.

The temperature of the target region of fatty tissue 285 can optionally be detected during the exemplary heating procedure using the sensor 290, and the flow rate and/or temperature of the heated fluid can be controlled based on a signal provided by the sensor 290 to provide a more accurate temperature within the targeted region of fatty tissue 285. For example, the fatty tissue 285 can be heated to a temperature between about 42 °C and about 48 °C, although higher or lower temperatures may also be used. As described herein, target regions located in other types of tissue can also be heated using the exemplary techniques and apparatus described herein.

In further exemplary embodiments of the present disclosure, the method can further include aspirating a portion of the heated fatty tissue 285 and/or heated fluid through the needles 220 after the heated fluid is introduced to the tissue 285 through the needles 220. The aspiration can be performed, for example, after a particular time interval following the introduction of the heated fluid. In certain exemplary embodiments, the fatty tissue 285 can be mixed with the hot fluid and heated to a higher temperature (e.g., greater than about 48 °C) followed by aspiration of the heated mixture after a short time interval to avoid causing significant amounts of local necrosis or fibrosis in the fatty tissue 285.

Any of the exemplary tissue heating, fat damaging and/or fat removal techniques described herein in accordance with the present disclosure can be performed in a single treatment, or by multiple treatments performed either consecutively during one session (e.g., providing volumes of heated fluid through the needles 220 a plurality of
times at particular time intervals), or at longer intervals over multiple sessions. The tissue at a plurality or range of depths can be heated and/or aspirated based on a single insertion of the needle array by adjusting the lengths of the needles within the tissue. Multiple treatments can be performed at a single target region using multiple insertions of the needle arrays described herein, or over a larger area by inserting a needle array in several proximal areas of the skin, and performing the heating and optional aspiration techniques described herein in each area. Individual or multiple treatments of a given region of tissue can be used to achieve a desired amount of thermal damage and/or particular cosmetic or therapeutic effects.

The foregoing merely illustrates the principles of the invention. Various combinations, modifications and alterations of features of the described embodiments will be apparent to those skilled in the art in view of the teachings herein. It will thus be appreciated that those skilled in the art will be able to devise numerous techniques which, although not explicitly described herein, embody the principles of the present disclosure and are thus within the spirit and scope of the invention. All patents and publications cited herein are incorporated herein by reference in their entireties.
CLAIMS

WHAT IS CLAIMED IS:
1. An apparatus for heating tissue, comprising:
   a base;
   a plurality of hollow needles coupled to the base, wherein the hollow needles
   are structured to be inserted simultaneously to one or more predetermined depths within
   the tissue, and wherein the hollow needles are structured to direct a heated fluid into at
   least one portion of the tissue.
2. The apparatus of claim 1, wherein the heated fluid has a temperature that is greater
   than a temperature of the tissue.
3. The apparatus of any of claims 1 and/or 2, wherein at least one of the hollow needles
   comprises a thermally insulating material.
4. The apparatus of any of claims 1-3, wherein at least one of the hollow needles
   comprises at least one of a metal material, a metal alloy, a polymer, a ceramic, a Teflon®
   material and/or a semiconductor.
5. The apparatus of any of claims 1-4, wherein at least one of the hollow needles
   includes a plurality of openings proximal to a distal end thereof.
6. The apparatus of any of claims 1-5, wherein each of the hollow needles has
   substantially the same length.
7. The apparatus of any of claims 1-5, wherein at least two of the hollow needles have a
   different length with respect to one another.
8. The apparatus of any of claims 1-7, wherein a length of at least one of the hollow
   needles extending from a lower surface of the base is at least about 1 mm.
9. The apparatus of any of claims 1-7, wherein a length of at least one of the hollow
   needles extending from a lower surface of the base is between about 1 mm and about 5
   mm.
10. The apparatus of any of claims 1-7, wherein a length of at least one of the hollow
    needles extending from a lower surface of the base is greater than about 5 mm.
11. The apparatus of any of claims 1-10, wherein each of the hollow needles is
    substantially parallel to another one of the hollow needles.
12. The apparatus of any of claims 1-11, wherein a distance between adjacent ones of the
    hollow needles is less than about 10 mm.
The apparatus of any of claims 1-11, wherein a distance between adjacent ones of the hollow needles is less than about 8 mm

The apparatus of any of claims 1-11, wherein a distance between adjacent ones of the hollow needles is less than about 5 mm

The apparatus of any of claims 1-14, wherein the hollow needles include at least 10 hollow needles

The apparatus of any of claims 1-14, wherein the hollow needles include at least 30 hollow needles

The apparatus of any of claims 1-14, wherein the hollow needles include at least 50 hollow needles

The apparatus of any of claims 1-17, further comprising a vibrating arrangement that is mechanically coupled to at least one of the base and/or at least one of the hollow needles

The apparatus of any of claims 1-18, wherein the apparatus further comprises a movable plate provided in a proximity to the base such that the hollow needles pass through the movable plate, and wherein a distance between the movable plate and the base is modifiable such that at least one length of the hollow needles extending from a lower surface of the movable plate is adjustable to a particular length

The apparatus of any of claims 1-19, further comprising a conduit provided in communication with a proximal portion of at least one of the hollow needles, wherein the conduit is structured to direct the heated fluid into the plurality of hollow needles

The apparatus of any of claims 1-20, wherein a distal end of each of the hollow needles has a sharp point configured to facilitate an insertion of the hollow needles into the tissue

The apparatus of any of claims 1-21, wherein the base is provided as at least a portion of at least one of a housing and/or a handpiece

The apparatus of any of claims 1-21, wherein the base is structured to be coupled to at least one of a housing and/or a handpiece

The apparatus of any of claims 1-23, further comprising a temperature sensing arrangement, wherein at least a portion of the temperature sensing arrangement is provided in a location proximal to a distal portion of at least one of the hollow needles
25. The apparatus of claim 24, wherein a temperature of the heated fluid is controlled at least in part on a signal provided by the temperature sensing arrangement.

26. The apparatus of any of claims 1-25, further comprising a reservoir structured to hold the heated fluid, wherein the reservoir is provided in communication with a proximal portion of at least one of the hollow needles.

27. The apparatus of claim 26, further comprising a temperature control arrangement configured to at least one of control and/or maintain a particular temperature of the fluid within the reservoir.

28. The apparatus of any of claims 1-27, further comprising a valve arrangement configured to at least one of control and/or regulate a flow of the heated fluid into a proximal end of at least one of the hollow needles.

29. The apparatus of any of claims 1-28, wherein the proximal portions of the hollow needles are configured to communicate with a vacuum source to facilitate an aspiration of at least a portion of the heated liquid directed into the tissue through the hollow needles.

30. The apparatus of claim 29, further comprising a vacuum valve arrangement provided in communication with the hollow needles that is configured to control a rate of the aspiration of the heated fluid using the vacuum source.

31. The apparatus of any of claims 1-30, wherein the tissue comprises at least a portion of a hair follicle.

32. The apparatus of any of claims 1-30, wherein the tissue comprises a tumor.

33. The apparatus of any of claims 1-30, wherein the tissue comprises a fatty tissue.

34. The apparatus of claim 35, wherein the apparatus is further configured to aspirate at least a portion of the fatty tissue.

35. The apparatus of any of claims 1-34, wherein the heated fluid comprises at least one of a saline solution, an anti-inflammatory agent, an anesthetic agent and/or an emulsifying agent.

36. The apparatus of any of claims 1-35, wherein a diameter of each of the hollow needles is less than about 1000 µm.

37. The apparatus of any of claims 1-35, wherein a diameter of each of the hollow needles is less than about 800 µm.

38. The apparatus of any of claims 1-35, wherein a diameter of each of the hollow needles is less than about 500 µm.
39. The apparatus of any of claims 1-38, wherein the at least one portion of the tissue is proximal to at least a portion of the needles.

40. A method for heating tissue, the method comprising:
    simultaneously inserting a plurality of hollow needles into the tissue to position portions of the hollow needles at least one of within and/or proximal to at least a portion of the tissue; and
    directing a heated fluid through the hollow needles such that at least a portion of the heated fluid enters the tissue through at least one opening provided at the portions of the hollow needles,
    wherein at least one of a temperature and/or a volume of the heated fluid directed into the tissue is selected to heat at least a portion of the tissue to a temperature within a predetermined temperature range.

41. The method of claim 40, wherein at least some of the hollow needles are affixed to a base and are substantially parallel to a further one of the hollow needles.

42. The method of any of claims 40 and/or 41, further comprising controlling at least one of a temperature and/or a volume of the heated fluid directed into the tissue to heat at least a portion of the tissue to the temperature within the predetermined temperature range.

43. The method of any of claims 40-42, further comprising causing an aspiration of at least a portion of the heated fluid that is directed into the tissue.

44. The method of claim 43, wherein the tissue comprises a fatty tissue, and further comprising causing an aspiration of at least a portion of the heated fatty tissue.

45. The method of any of claims 40-44, wherein the portions of the needles are distal portions of the needles.
FIG. 5A

FIG. 5B

FIG. 6
**INTERNATIONAL SEARCH REPORT**

**A. CLASSIFICATION OF SUBJECT MATTER**

* A61M 37/00(2006.01), A61M 5/158(2006.01), A61M 5/32(2006.01)1

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC A61M 37/00

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Korean Utility models and applications for Utility models since 1975

Japanese Utility models and applications for Utility models since 1975

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

KOMPASS (KIPO internal) & Keywords needle, tissue, heating

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>US 5,693,029 A (Leonhardt, Howard J) 02 DECEMBER 1997 See Claims 1-17, Figures 1-5</td>
<td>1-3</td>
</tr>
</tbody>
</table>

☐ Further documents are listed in the continuation of Box C  ☒ See patent family annex

* Special categories of cited documents
  * "A" document defining the general state of the art which is not considered to be of particular relevance
  * "E" earlier application or patent but published on or after the international filing date
  * "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of citation or other special reason (as specified)
  * "O" document referring to an oral disclosure, use, exhibition or other means
  * "P" document published prior to the international filing date but later than the priority date claimed

'T' later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

'X' document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

'Y' document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

'&' document member of the same patent family

Date of the actual completion of the international search

27 OCTOBER 2009 (27 10 2009)

Date of mailing of the international search report

28 OCTOBER 2009 (28.10.2009)

Name and mailing address of the ISA/KR

[Logo]

Korean Intellectual Property Office
Government Complex-Daejeon, 139 Seonsa-ro, Seogu, Daejeon 302-701, Republic of Korea

Faxsimile No 82-42-472-7140

Authorized officer

HAN, SANG SOO

Telephone No 82-42-481-8648

Form PCT/ISA/210 (second sheet) (July 2008)
**INTERNATIONAL SEARCH REPORT**

**Box No. II  Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons

1. [✓] Claims Nos 40-45
   
   because they relate to subject matter not required to be searched by this Authority, namely
   
   Claim 40-45 relates to a method for heating tissue, which falls into the category of methods for treatment of the human body by surgery or therapy as well as diagnostic methods [Article 17(2)(a)(i), Rule 39I(iv) PCT]

2. [✓] Claims Nos 27, 30, 34, 44
   
   because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically
   
   Claims 27, 30, 34, 44 are in reference to claims that are multiple dependent claims, which are not subjected to the meaningful search in accordance with the second and the third sentence of Rule 4(a) [Article 17(2)(a)(n), Article 6 PCT]

3. [✓] Claims Nos 4-26, 28-29, 31-33, 35-39, 43, 45
   
   because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 4(a)

**Box No. III  Observations where unity of invention is lacking (Continuation of item 3 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims

2. [✓] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims, it is covered by claims Nos

**Remark on Protest**

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation

[ ] No protest accompanied the payment of additional search fees

Form PCT/ISA/210 (continuation of first sheet (2)) (July 2008)
<table>
<thead>
<tr>
<th>Patent document cited in search report</th>
<th>Publication date</th>
<th>Patent family member(s)</th>
<th>Publication date</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>CA 2444505 A1</td>
<td>24.10.2002</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DE 602 16436 D1</td>
<td>11.01.2007</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DE 602 16436 T2</td>
<td>04.10.2007</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EP 138 1418 B1</td>
<td>29.11.2006</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EP 138 1418 A2</td>
<td>21.01.2004</td>
</tr>
<tr>
<td></td>
<td></td>
<td>US 2005-0197633 A1</td>
<td>08.09.2005</td>
</tr>
<tr>
<td></td>
<td></td>
<td>US 06969373 B2</td>
<td>29.11.2005</td>
</tr>
<tr>
<td></td>
<td></td>
<td>wO 0208-3228A3</td>
<td>10.04.2003</td>
</tr>
<tr>
<td></td>
<td></td>
<td>wO 2002-083228 A2</td>
<td>24.10.2002</td>
</tr>
<tr>
<td></td>
<td></td>
<td>wO 2002-083228 A3</td>
<td>24.10.2002</td>
</tr>
<tr>
<td></td>
<td></td>
<td>US 2004-00 15219 A1</td>
<td>22.01.2004</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CA 2444505 A1</td>
<td>24.10.2002</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DE 602 16436 D1</td>
<td>11.01.2007</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DE 602 16436 T2</td>
<td>04.10.2007</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EP 138 1418 B1</td>
<td>29.11.2006</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EP 138 1418 A2</td>
<td>21.01.2004</td>
</tr>
<tr>
<td></td>
<td></td>
<td>US 2005-0197633 A1</td>
<td>08.09.2005</td>
</tr>
<tr>
<td></td>
<td></td>
<td>wO 0208-3228A3</td>
<td>10.04.2003</td>
</tr>
<tr>
<td></td>
<td></td>
<td>wO 2002-083228 A2</td>
<td>24.10.2002</td>
</tr>
<tr>
<td></td>
<td></td>
<td>wO 2002-083228 A3</td>
<td>24.10.2002</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EP 1083959 A1</td>
<td>21.03.2001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>wO 1997-002859 A1</td>
<td>30.01.1997</td>
</tr>
</tbody>
</table>