# What Happens to the Fat After Treatment With the UltraShape™ Device

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## INTRODUCTION

Fat is nature's way of storing excess energy. Fat is very efficient in storing energy as it takes up very little space and does not require a lot of water when stored in a cell. Figure 1 presents a typical histopatho-logical specimen of human fat tissue. What appears as empty cells are in fact fat–filled cells. Up to 75% of the volume of fat cells is occupied with what we call fat (triglycerides).

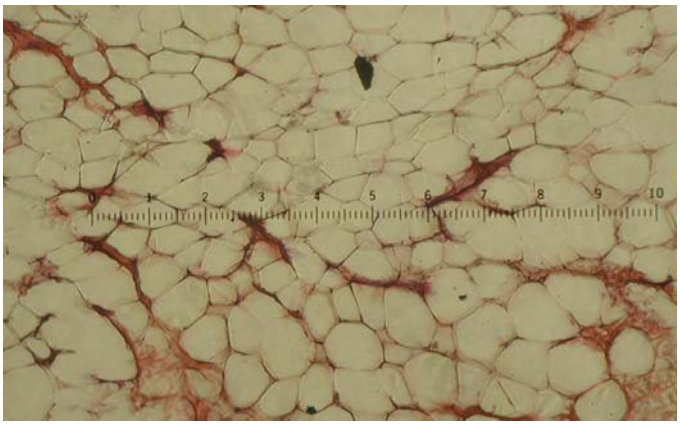


**Fig. 1**: Typical adipose tissue (Hematoxyin-Eosin staining)

When fat tissue is treated by the UltraShape™ device, the focused ultrasound beam is directed towards a specific area within the fat layer. The ultrasound wave causes mechanical disruption of the membranes of the fat cells, sparing the blood vessels, peripheral sensory nerves and connective tissue. Since the effect is focused to a specific depth, overlaying skin is not damaged. Figures 2 and 3 depict histopathological tissue samples after UltraShape treatment, showing a clear differentiation between areas of disrupted fat tissue and surrounding intact fat tissue, connective tissue, blood vessels and dermis.

The most common question that arises is the fate of the fat previously contained in the adipose cells, after the cell membrane is broken. This paper aims at describing the mechanisms of fat absorption following the cell disruption by UltraShape™ treatment.

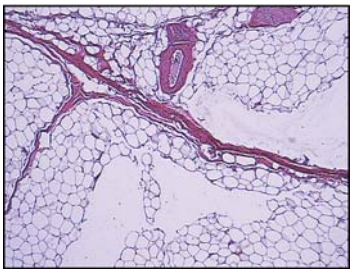


**Fig. 2**: Histopathological sample immediately following UltraShape treatment (Hematoxylin-Eosin staining, x50). Image shows disrupted fat cells with no damage to adjacent blood vessels.

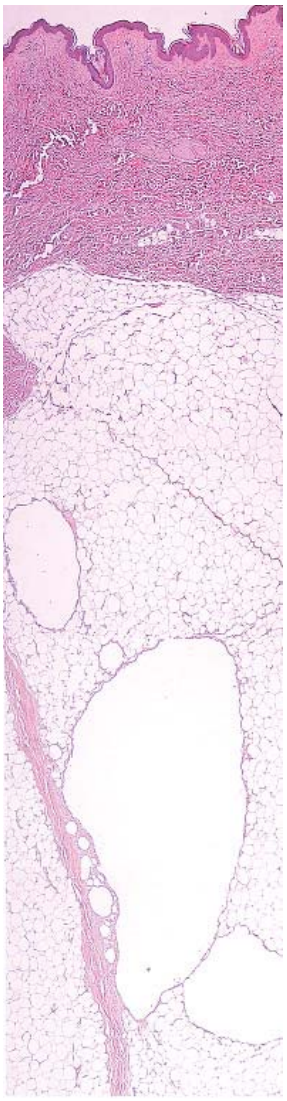


**Fig. 3**: Histopathological sample immediately after UltraShape treatment (Hematoxylin-Eosin staining, x25). Note damage to fat cells (empty areas) and intact skin and connective tissue.

## FAT CLEARANCE MECHANISM

Fat, inside fat cells, exists in the form of triglycerides. A triglyceride molecule is comprised of three fatty acids attached to a glycerol backbone. When the fat cell membrane is destroyed, triglycerides are released into the interstitial fluid between the cells.

The presence of large amounts of triglycerides, in interstitial fluid compartments, has no natural correlate. When outside the fat cell, triglycerides are normally packaged in discrete lipoprotein particles – a combination of apolipoproteins and lipids, cholesterol, triglycerides, and cholesteryl esters. A series of metabolic pathways direct the trafficking of water insoluble molecules of cholesterol and triglyceride through the water-based circulatory system and to the interstitial fluid space[1]. During the passage through the arteries and interstitial space, lipoprotein-bound triglycerides are catabolized to free fatty acids and glycerol molecules.

There is little or no animal or clinical data describing the distribution and temporal processing of free triglycerides released from traumatized adipocytes. The only clinical correlate may be trauma cases of massive areas of soft tissues (car accidents, burns, etc).

This discussion focuses on the interstitial compartment and the metabolism of triglycerides, free fatty acids and glycerol. It is well established that interstitial fluid compartments contain lipoproteins, biological signals and chemical analytes that all interact and engage cells through cell surface membrane receptors or processes (phagocytosis, etc). The kinetic features of the interstitial compartment are now being understood for normal analyte, as about 42% of the total body water is extracellular[2].

***Are triglyceride molecules present in the interstitial fluid metabolized to free fatty acids and glycerol?*** According to the literature, it seems very reasonable to assume that triglycerides are immediately processed by lipoprotein lipase (LPL), an enzyme bound to adipocytes[3,4]. *In vitro* studies have shown that triglyceride presented as emulsions and not in lipoprotein particles are readily hydrolyzed by LPL to glycerol and free fatty acids[5,6].

***Glycerol is a water soluble molecule and requires no chaperone or carrier through interstitial fluids or the circulatory system.*** A short term increase in glycerol concentration following UltraShape treatment appears reasonable but has not been directly measured. However, interstitial levels of glycerol are similar to plasma levels[2]. To date, no clinically significant elevation of plasma glycerol levels has been reported in any UltraShape subject. One may extrapolate that interstitial glycerol levels were not significantly elevated in this compartment or sequestered subsequent to UltraShape treatments.

Free fatty acids are not readily immiscible in water and the transport of these molecules is accomplished by albumin. Albumin, present in interstitial fluid and circulation, has the capacity to bind 2-3 molecules of free fatty acid per molecule[7]. Recently, a differentially radiolabeled triglyceride was injected into the circulatory system of eight subjects[8]. The glycerol and fatty acids moieties had different radiolabels which allowed the kinetic examination of glycerol and fatty acids fates. In the forearm, systemic clearance and forearm fractional extraction of glycerol (59%) was greater than that of oleate (14%). Equal systemic and forearm fractional release levels of LPL-generated were observed; again validating the equilibrium that exists between these two water compartments for glycerol. This study suggested that LPL-mediated fatty acid uptake is an inefficient process, but that muscle is more effective than adipose tissue.

Free fatty acids released during the treatment will eventually be delivered to the liver. In the liver, there is no distinction between fatty acids that originate from disrupted adipocytes, those taken from adipocytes due to physiological needs or those originating from a meal consumed several hours ago. In other words, free fatty acids released from the UltraShape-treated fat cell are being processed in normal pathways that nature has evolved for the transport of fat.

A very simplified illustration (next page) depicts the normal transport of cholesterol and triglyceride in our circulatory system. Triglyceride (TG) is primarily ingested during the dietary processes [stomach and intestine] and transported by chylomicrons through the capillaries (red arrow) and lymph where a large portion is broken down into free fatty acids and glycerol. Any unprocessed TG in chylomicrons is taken up by the liver. A second source of triglyceride is through production in the liver from excess free fatty acids and glycerol. The impor-tant cell type that stores TG as an energy bank or depot is the fat cell, or in more scientific terms – an adipocyte.

UltraShape (red box) disrupts fat cells by breaking down the cell membranes, causing the release of TG (green) from the cells. A great portion of TG is probably broken into free fatty acids and glycerol because of the enyzme, lipoprotein lipase, on the fat cell membrane walls.

The free fatty acids being relatively insoluble in water bind to albumin and are slowly transported to the liver or other tissues that need these molecules as building blocks or energy.

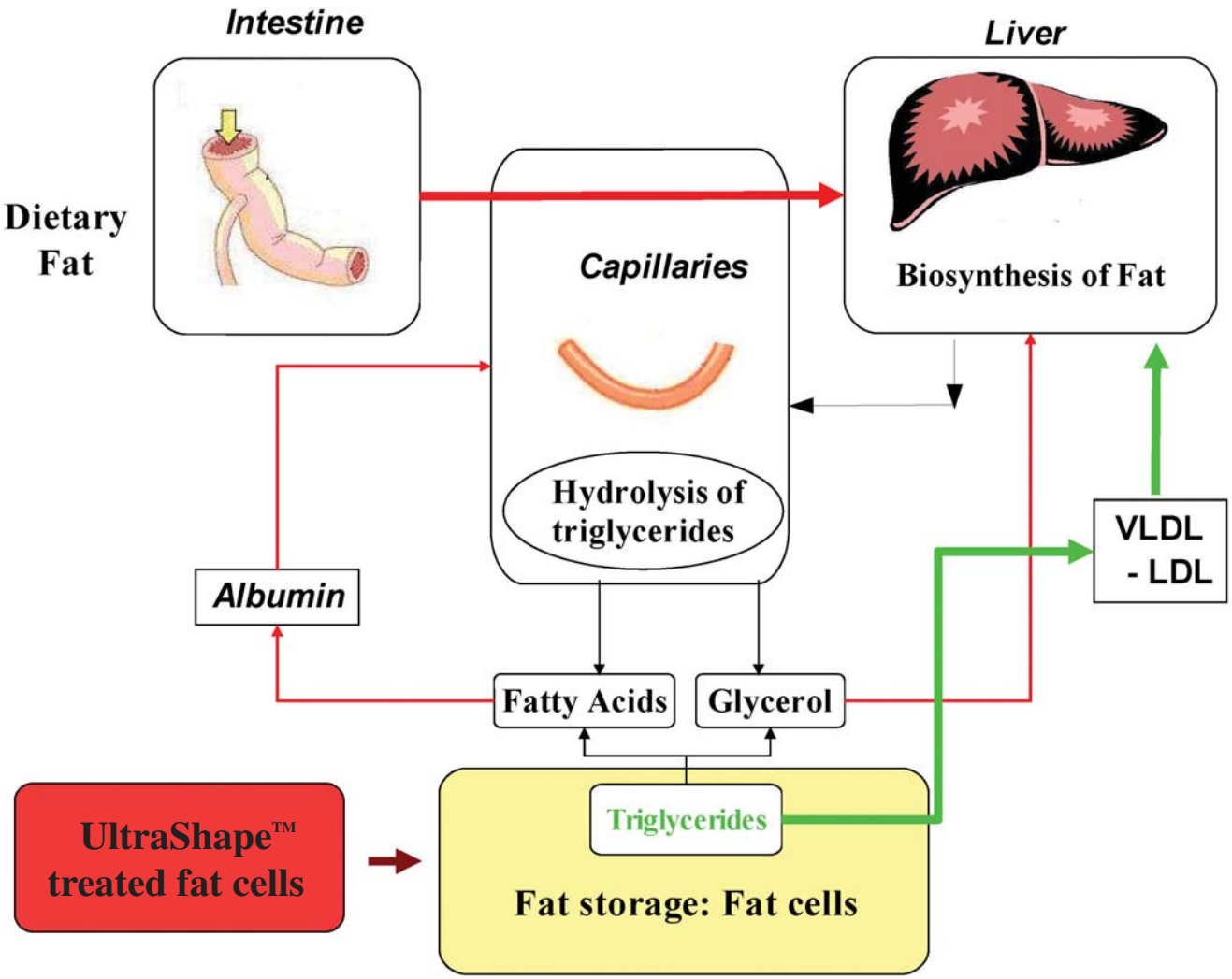
Glycerol is soluble in water and is transported to the liver or to other cells that could use this molecule. The free glycerol equilibrates among both the interstitial fluid compartment (tissue fluids) and systemic (blood) fluid compartments.

If the released TG (green) is not broken down, it may bind to very low density lipoprotein particles (VLDL) found in the lymph. VLDL is further processed to other lipoprotein classes (IDL, LDL) and ultimately transported to the liver for recycling back to free glycerol and free fatty acids.

All of these pathways have enormous capacity and fast response times in terms of handling TG, as witnessed in the removal of TG in 3-4 hrs from a 2000 cal milkshake.

**SUMMARY**

In conclusion, the released TG or its derivatives are processed by known metabolic pathways. No unnatural or new metabolic pathways are required for the body to process the released TG. In addition, TG from adipocytes treated by UltraShape ultimately travels to the liver, where it is recycled to meet the continuing demands of the body.



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