



Medical University of Graz

# Differences in skin carotenoid level with regard to subcutaneous adipose tissue thickness in patients with anorexia nervosa

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# Introduction – Why dealing with anorexia nervosa?

## ▶▶ Anorexia nervosa

- severe psychiatric disease
- characterized by self-induced weight loss, BMI < 17.5 kg/m<sup>2</sup>, impaired self-perception WHO ICD-10
- affects primarily young females (prevalence ~0.5% among 15-35 year old women) *Herpertz et.al. Springer 2015*
- high relapse rates (~ 30% within the first year after inpatient treatment) *Herpertz et.al. Springer 2015*
- high mortality rate (5-10% 10 years after diagnosis) *Treasure et al. Lancet 2010*

## ▶▶ Treatment strategies

- aim for rapid weight restoration
- mostly based on high caloric diet and activity restriction
- lack of evidence based guidelines *Yager et.al. Focus 2014*

## ▶▶ Pathophysiological mechanisms

- not completely clear yet

# Background

## Pilot-Study: Energy sensing in anorexia nervosa



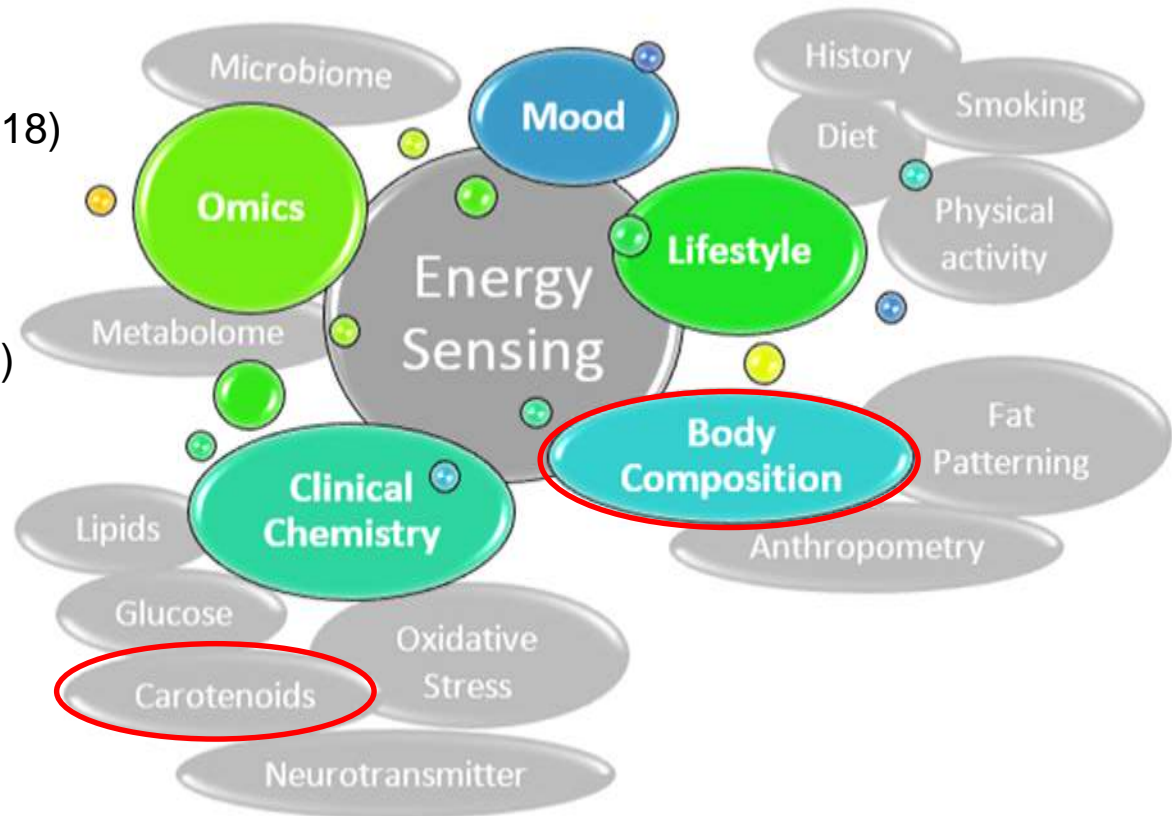
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▶▶ Comparison of energy sensing parameters in groups with different energy status

▶▶ Study population (n=107)

female, 18-40 years

- Anorexia nervosa patients (n=18)
  - BMI < 17.5
- Normal weight controls (n=27)
  - BMI 18.5 – 24.99
- Overweight participants (n=22)
  - BMI 25.0-29.99
- Obese participants (n=20)
  - BMI  $\geq$  30.0
- Athletes (n=20)
  - $\geq$  7 training hours per week
  - local level competitions



# Selection of an appropriate method for the assessment of body composition in very lean patients



## ▶▶ DXA:

- uses assumptions that are not appropriate for skinny persons
- partly results in „negative” amounts of body fat on parts of the body in slim people (as shown in some athletes)

*Ackland et.al. Sports. Med. 2012*

## ▶▶ MRI:

- Pixel size used in MRI scans is typically between 1.3 and 2 mm.
- AN patients are expected to have thinner fat layers at some body parts.

*Ackland et.al. Sports. Med. 2012*

## ▶▶ Others: Skinfolds, BIA

- Do not reach necessary accuracy and reliability

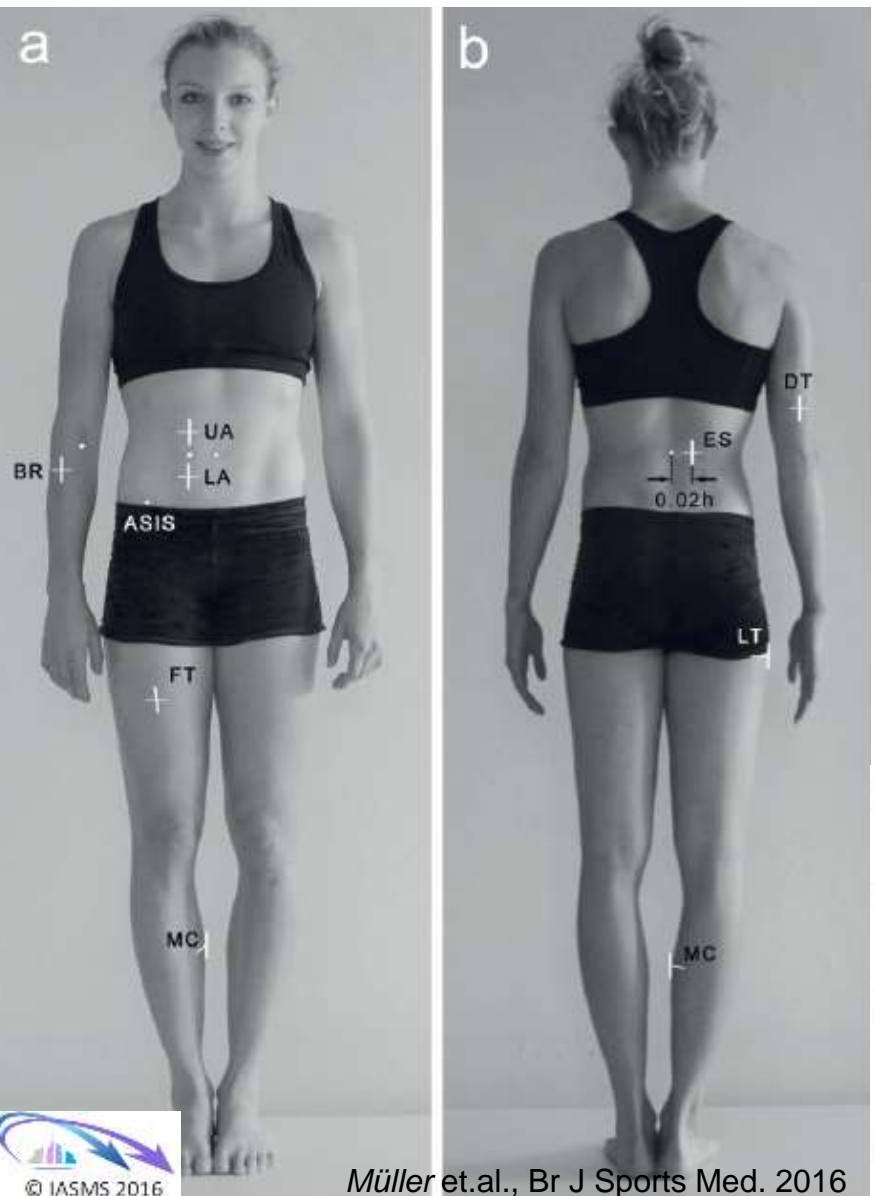
*Ackland et.al. Sports. Med. 2012*

## ▶▶ Ultrasound:

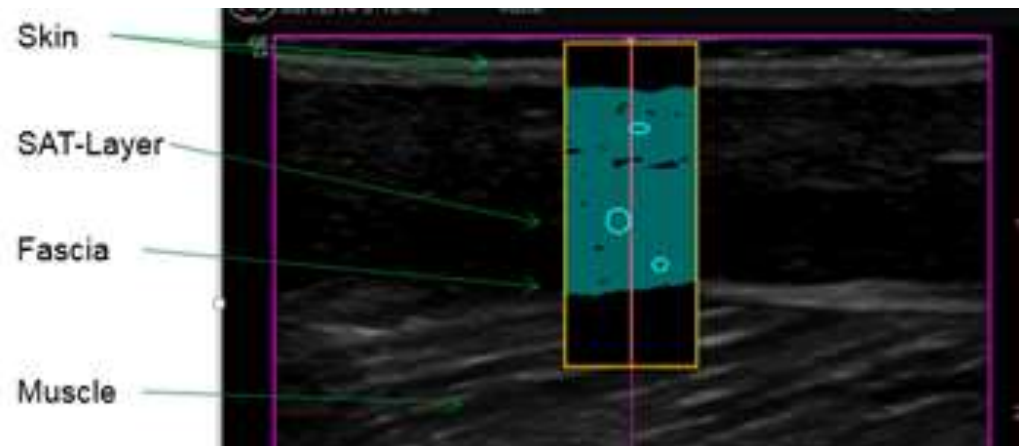
- Detection of layers < 1mm with high precision and accuracy

*Müller et.al. Br J Sports Med. 2016; Störchle et.al. Ultrasound Med. Biol. 2017*

# Ultrasound Measurement of subcutaneous adipose tissue (SAT)



- ▶▶ Measurement of eight standardized body sites by diagnostic ultrasound
- ▶▶ No compression of the fat layer
- ▶▶  $D_{INCL} = \text{SAT thickness sum (of 8 sites)}$

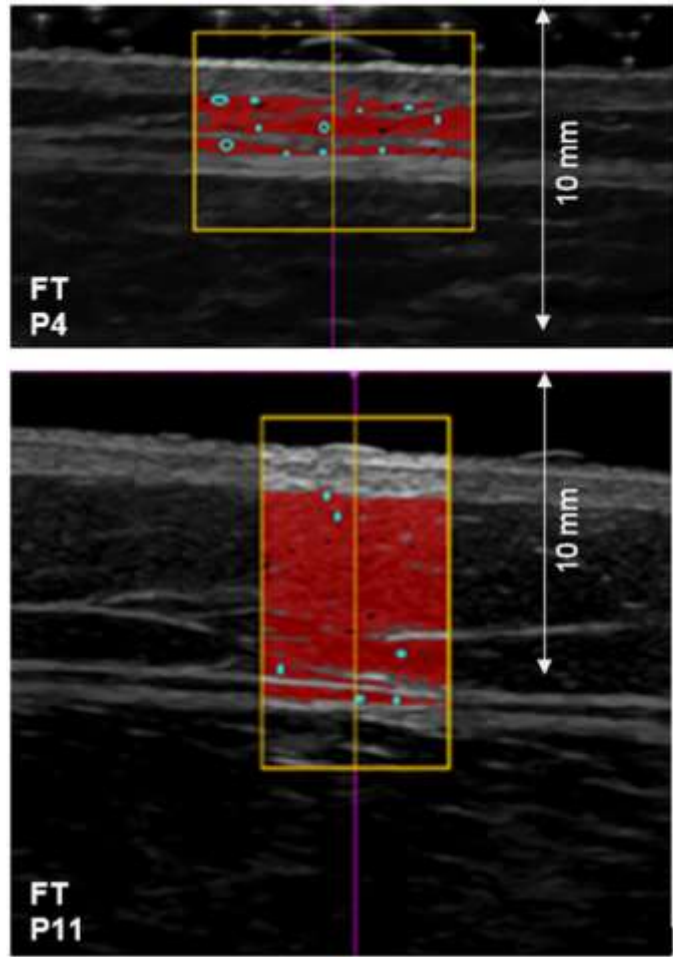




## Results of the ultrasound measurement

- ▶▶ AN patients with a BMI from 13.2 to 17.2 kg m<sup>-2</sup> were included
- ▶▶ We observed great differences in the amount of subcutaneous fat in BMI matched patients
  
- ▶▶ The study population was divided into two groups by the median of  $D_{\text{INCL}}$
- ▶▶ Only group 1 patients had extremely low SAT values
- ▶▶ The SAT amount of group 2 patients was sufficient

# Comparison of fat patterning in two AN patients with the same BMI at the measurement site front thigh (FT)



	BMI [kg m <sup>-2</sup> ]	$D_{INCL}$ [mm]	$d_{FT}$ [mm]
P4	14.5	9.0	1.7
P11	14.7	33.3	6.6

*unpublished data*

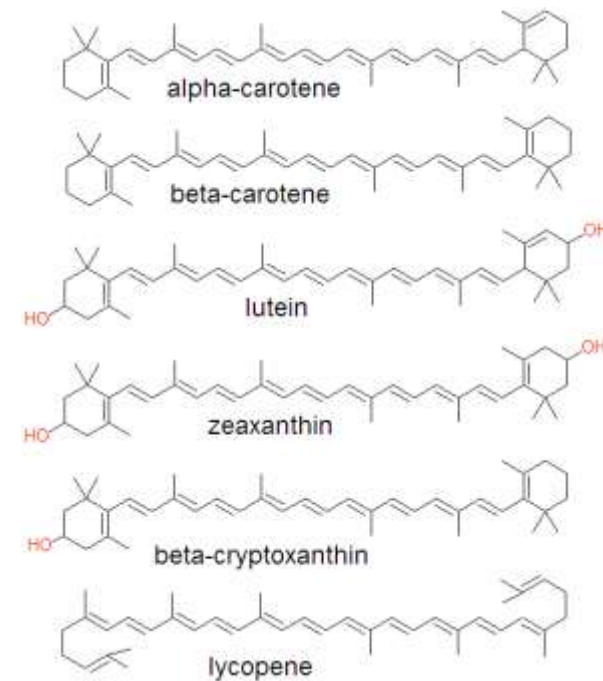
## What do these results suggest?

- ▶▶ If patients with almost the same BMI differ in their body fat mass, they must also differ in other body structures such as muscle, bone, organ mass etc.
  
- ▶▶ Based on this observation we were interested in further clinical differences between the two groups of anorexia nervosa patients.



# Background carotenoids

- ▶ Characteristics of carotenoids:
  - lipophilic C-40-based isoprenoid molecules
  - red, orange, yellow pigments produced by plants, microorganisms and fungi
- ▶ Main dietary sources: Fruits and vegetables
- ▶ Function of carotenoids in human:
  - pro-vitamin A
  - antioxidative properties
  - impact on gene expression and cell function
  - role in adipose tissue biology
- ▶ Transport and Storage of Carotenoids:
  - Directly connected to lipid metabolism
  - Stored in the liver, adipose tissue, skin, retina,...



*Bonet et.al., Arch. Biochem. Biophys. 2015*

*Bohn et.al., Mol. Nutr. Food Res. 2017*



# Hypercarotenemia in anorexia nervosa

## ▶▶ Recognized occurrence in AN patients

*Robby Am J Clin Nutr 1974, Boland Int J Eat Disord 2001 Mazzone N Engl J Med 2002*

## ▶▶ Characteristics

- high  $\beta$ -carotene plasma concentrations
- accumulation of carotenoids in the skin

## ▶▶ Possible causes

- high intake of carotenoid containing food
- normal intake with decreased requirement
- Hypercholesterinemia
- acquired error of carotenoid metabolism
  - disturbance of lipoprotein degradation
  - problems with storage of carotenoids due to reduced adipose tissue



*Mazzone et.al. N Engl J Med 2002*

## ▶▶ Pathophysiological mechanisms remain unclear yet.

# Methods for determination of carotenoids

## ▶▶ Skin carotenoids

- Resonance Raman Spectroscopy
  - Based on light absorbing properties of carotenoids
  - Provides a measure for the total concentration of carotenoids

*Ermakov et al. Arch Biochem Biophys 2015*

*Mayne et al. Arch Biochem Biophys 2013*

- Why detecting skin carotenoids?
  - Reflect carotenoid status appropriately
  - Easy, non-invasive application in clinical practice



## ▶▶ Plasma carotenoids

- HPLC analysis
- $\beta$ -Carotene

## Results Carotenoids

- ▶▶ Skin carotenoids differed significantly between the two groups
  - Group 1 patients had higher skin carotenoid values
  
- ▶▶ Plasma  $\beta$ -carotene concentration differed significantly between the two groups
  - Group 1 patients had higher plasma  $\beta$ -carotene values

## Additional information

- ▶ Higher oxidative stress in group 1 patients (TAC, TOC, oLab, EPA, MDA-LDL IgM)
- ▶ No differences regarding lifestyle behaviour and lipid-metabolism have been observed

## What do these results suggest?

- ▶ Hypercarotenemia in anorexia nervosa patients is probably linked to the patients body composition
  - The amount of remaining adipose tissue may influence the possibility of carotenoid storage
- ▶ Lower body fat was associated with higher carotenoids and higher oxidative stress
  - Indicates that carotenoids cannot be utilized adequately
- ▶ Hypercholesterinemia may play a minor role in hypercarotenemia

## Main findings

- ▶▶ We have observed pronounced differences in body fat in patients with anorexia nervosa
  - Subcutaneous adipose tissue thickness varied from extremely low to normal ranges
  - the group with higher body fat must have low muscle mass
- ▶▶ Patients with lower body fat had higher carotenoid status but also higher oxidative stress.

## Suggestions for the therapeutic approach

- ▶▶ Therapeutic approaches should be adopted according to the body composition of the patient
  - Implementation of body composition assessment and monitoring
  - Implementation of low energy turnover muscle strength training for those with higher fat and lower muscle mass
  - personalised nutritional therapy

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