

**Insulin-resistance in overweight women with breast cancer:  
effect of cytokines and body weight,  
before and after successful chemotherapy.**

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# **Introduction:**

**Malignancy is known to be an insulin-resistant state, possibly attributed to the action of multiple cytokines. Moreover, insulin resistance (IR) is a well-known condition in overweight persons, especially those with central obesity.**

## **Aim:**

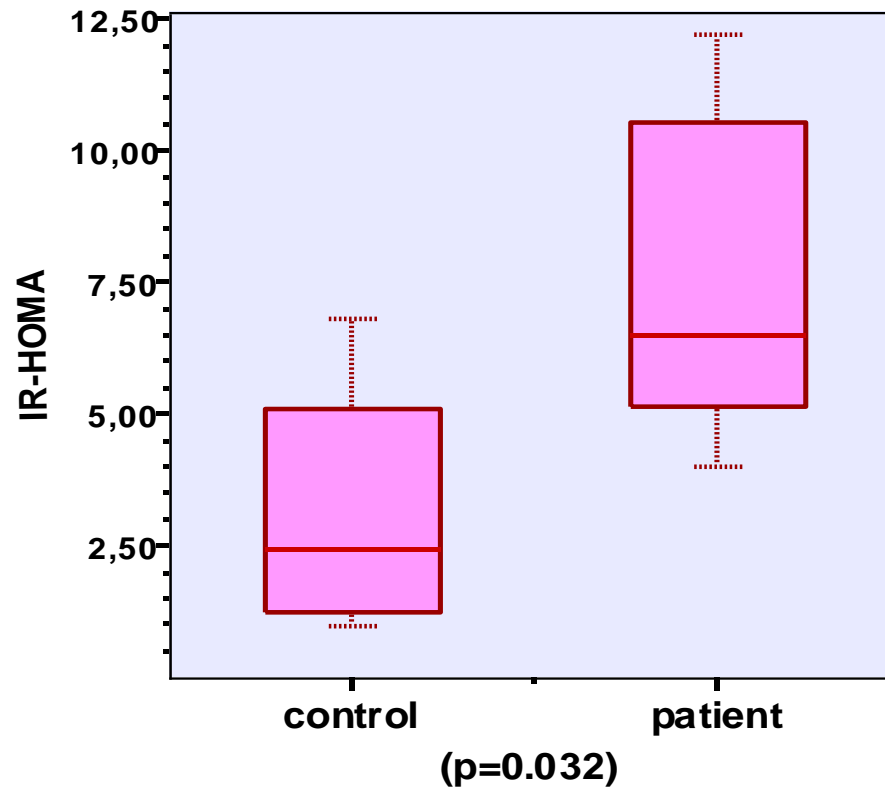
**To explore insulin resistance (IR), as well as certain growth factors and cytokine levels, in women suffering from breast cancer and to possibly prove:**

- a) their relationship with anthropometric measurements, BMI in particular, and**
- b) the change in IR when these patients are successfully treated.**

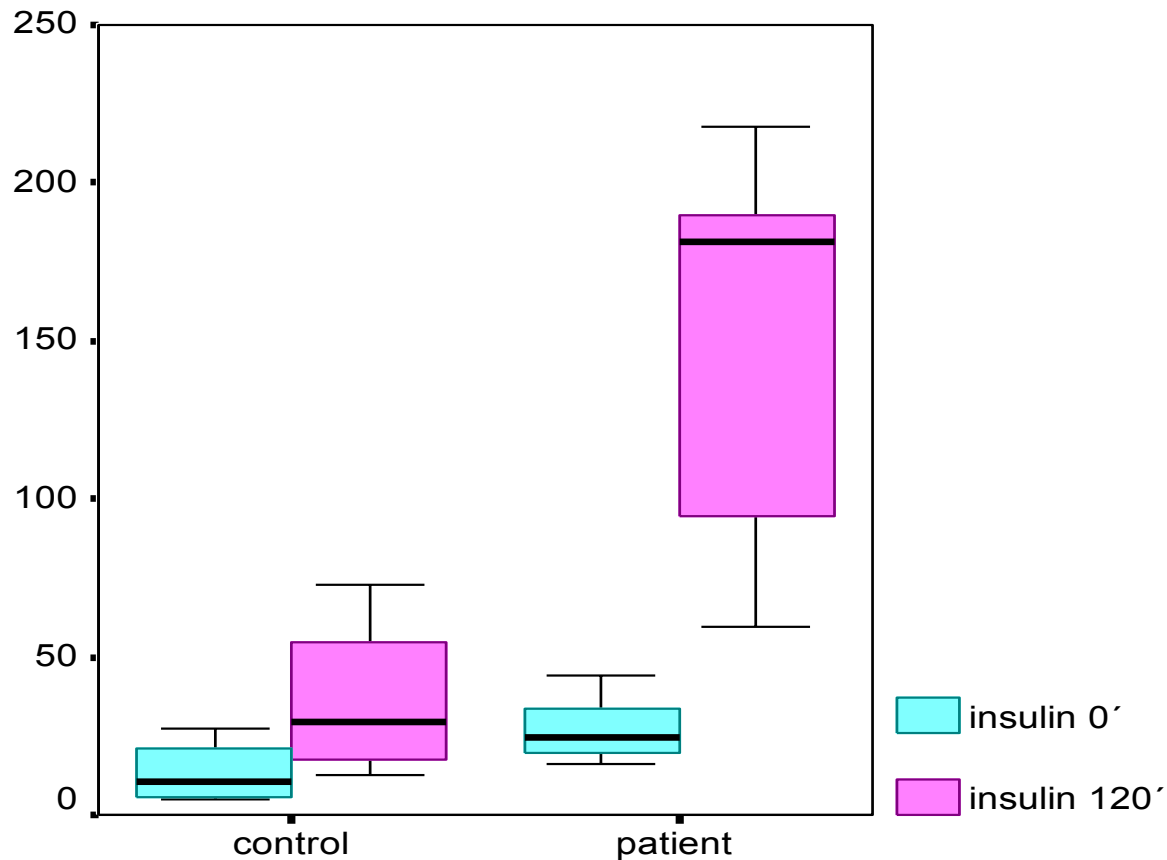
# **Methods:**

- ◆ **11 not (known) diabetic women, with stage IV breast cancer (hepatic metastases excluded), age  $62.45 \pm 8.43$ , BMI  $28.26 \pm 2.74$ , and 4 controls (BMI  $30.86 \pm 5.51$ ) were subjected to weight and height measurements for calculation of BMI, and OGTT with 75gr glucose.**
- ◆ **Blood glucose levels as well as insulin, leptin, IL-1, IL-6, IL-8, TNF- $\alpha$ , PDGF, VEGF and IGF-1 were measured before and 120 minutes after glucose administration. IR and  $\beta$ -cell function were calculated using HOMA method.**
- ◆ **Patients were subjected to the same measurements after 6 cycles of successful chemotherapy.**
- ◆ **Statistics included simple and paired t-test, Wilcoxon test, parametric and non-parametric correlation (r Pearson and r Spearman), multiple regression analysis and ANOVA for two-way interactions. Calculations were carried out using SPSS statistical package version 11.5. Results were considered significant when  $p < 0.05$ .**

# **Results:**



**Patients were found to be more insulin resistant than controls:  
(7.62±3.15 vs. 3.16±2.64, p=0.032)**

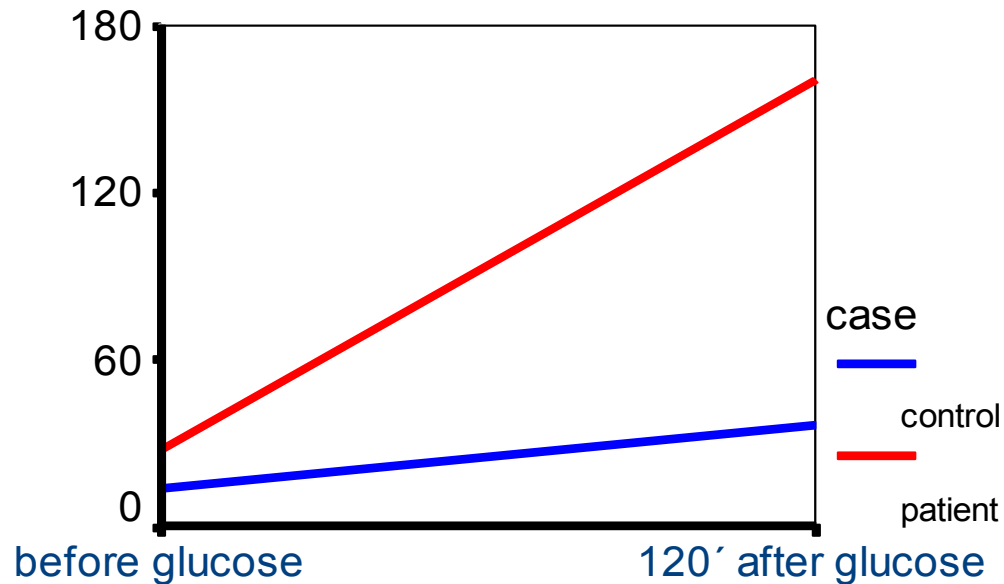


insulin 0':  $p=0.037$  - insulin 120':  $p=0.009$

**Patients had higher insulin levels than controls both before  
and after glucose administration**

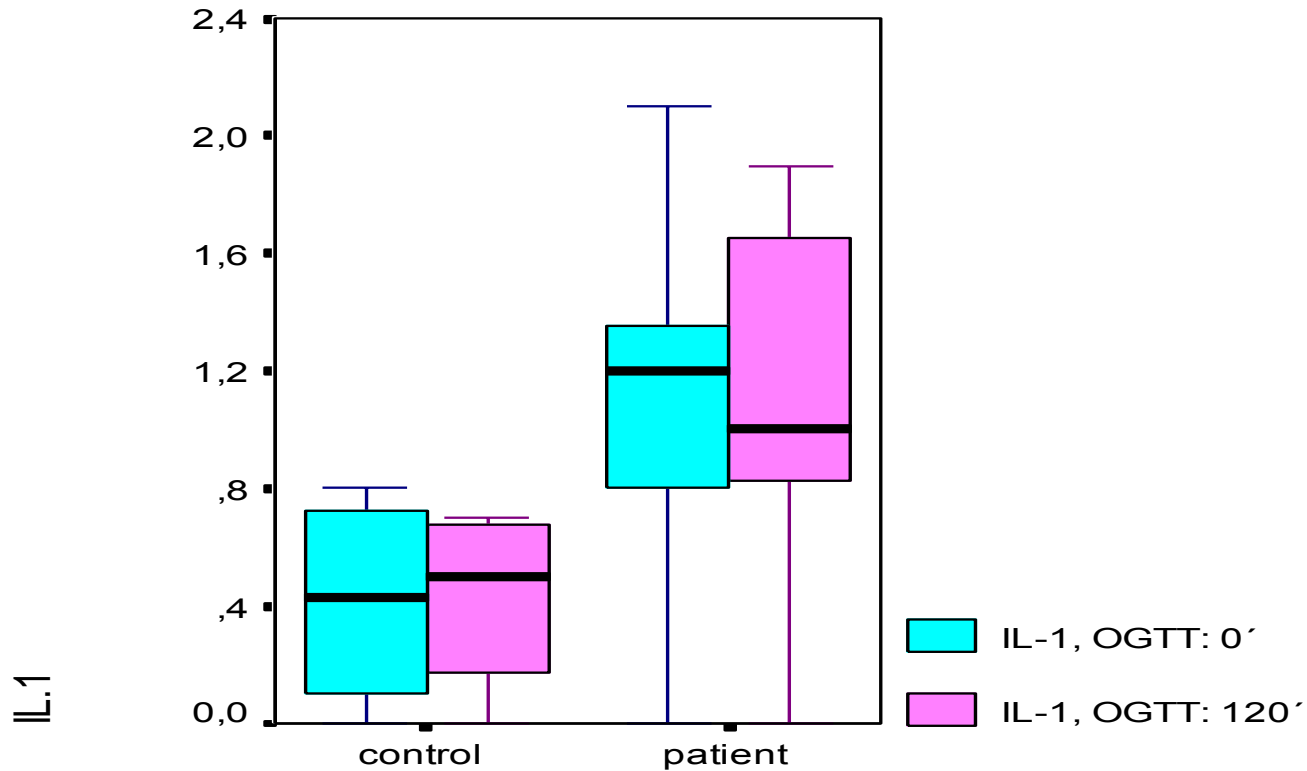
**( $23.35 \pm 8.93$  vs.  $13.55 \pm 10.27$ ,  $p=0.037$  and  
 $160.28 \pm 81.30$  vs.  $36.19 \pm 26.50$ ,  $p=0.009$ , respectively)**

# OGTT had a greater insulin response in patients than in controls (p=0.016)



**R square=60.4, F=15.766, Sig=0.000**

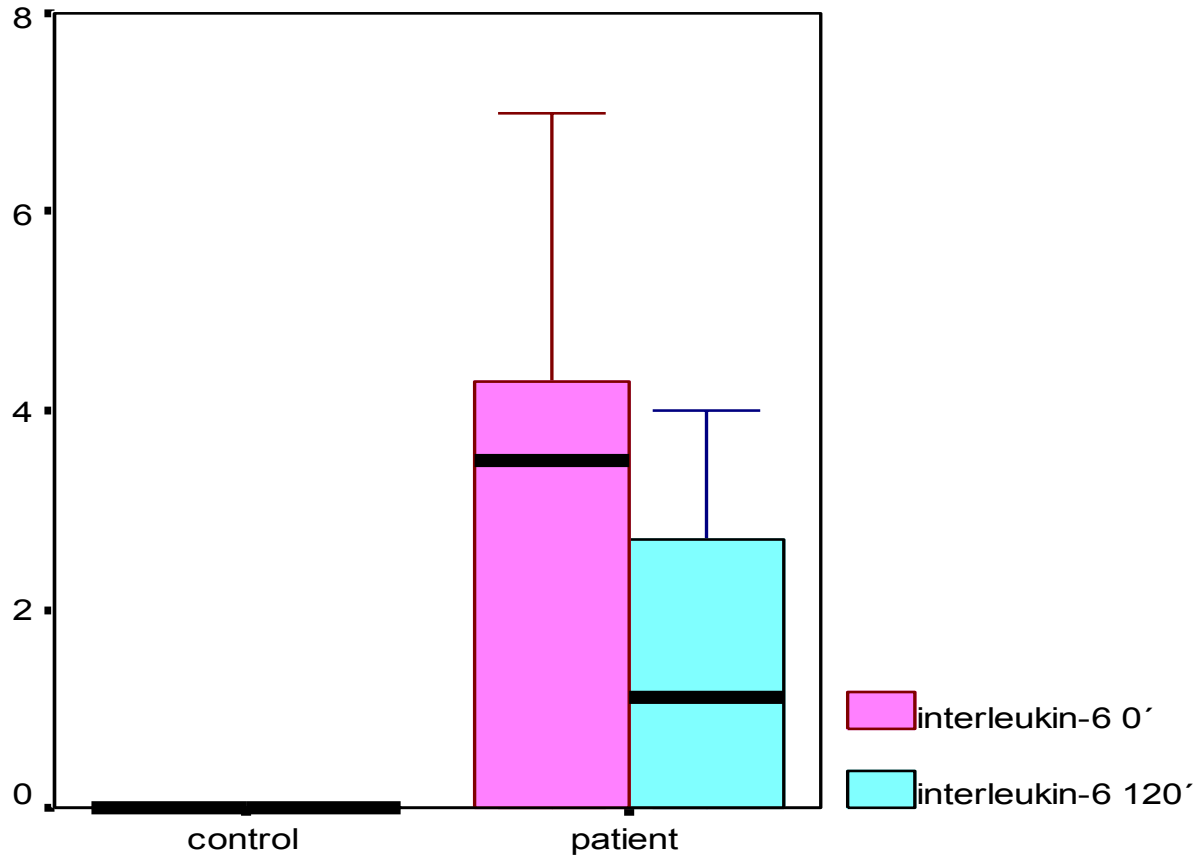
**Case: p=0.003, OGTT: p=0.001, case x OGTT: p=0.016**



(IL-1 0' :  $p=0.056$ , IL-1 120' :  $p=0.031$ )

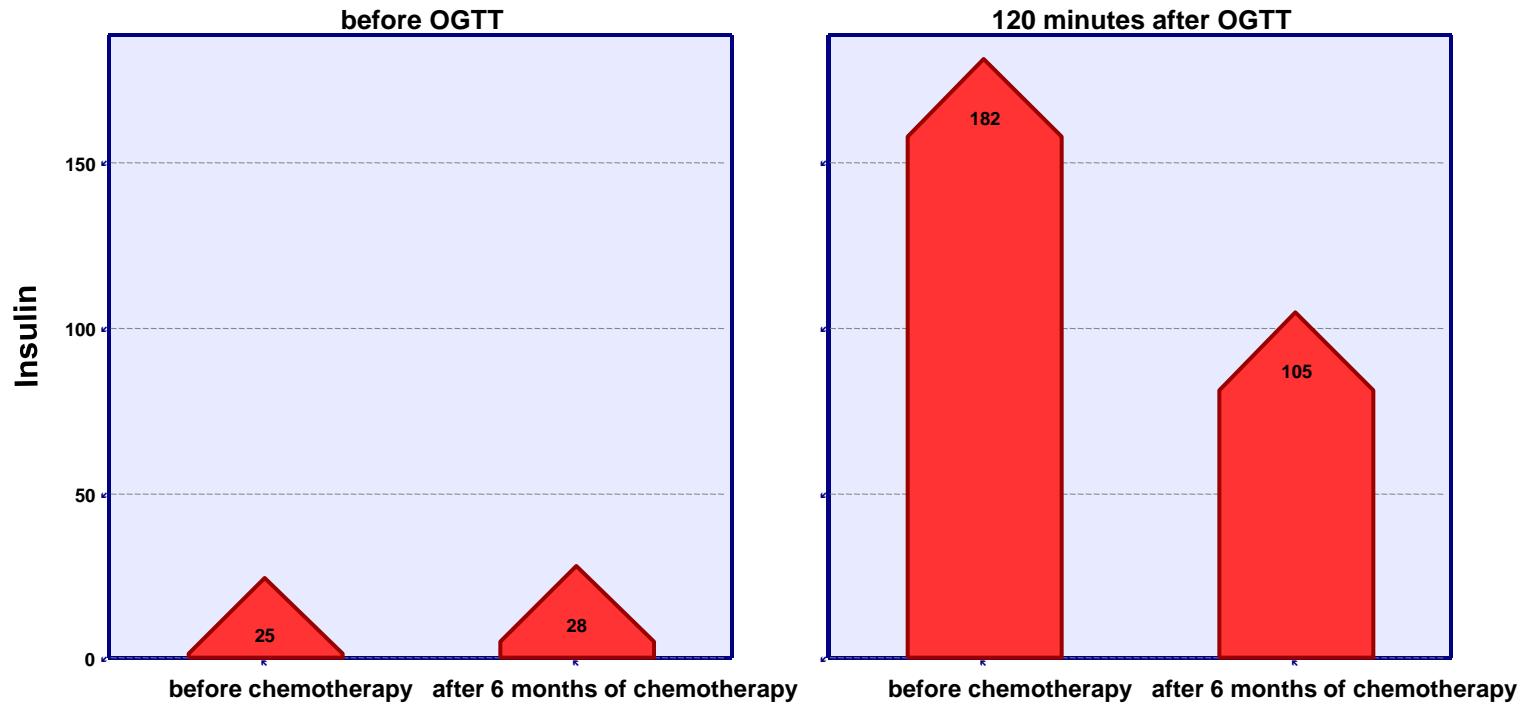
**Patients had higher interleukin-1 levels, than controls especially after glucose administration**



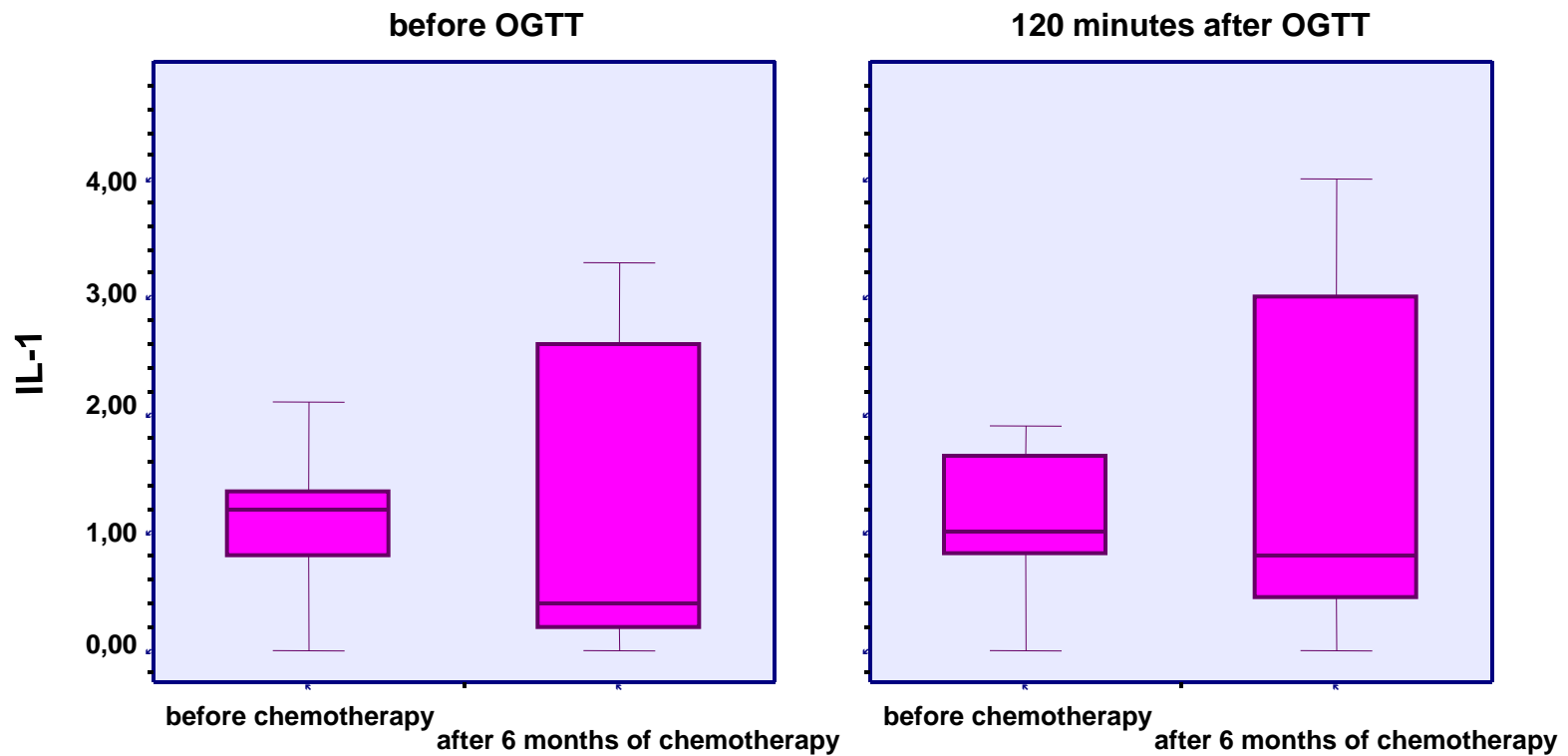


(IL-6 0':  $p=0.047$  IL-6 120':  $p=0.047$ )

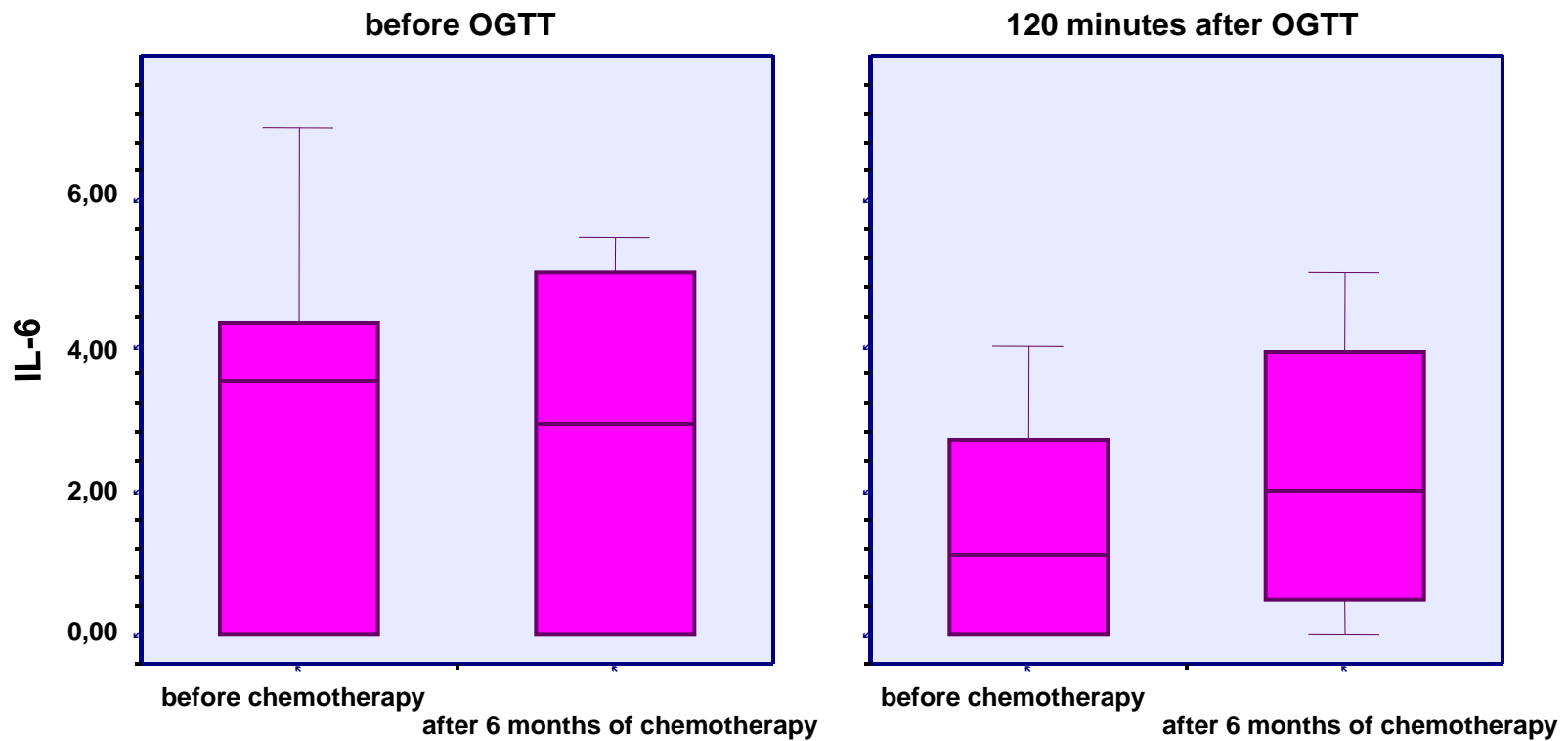
**Patients had higher interleukin-6 levels than controls both before and after glucose administration**



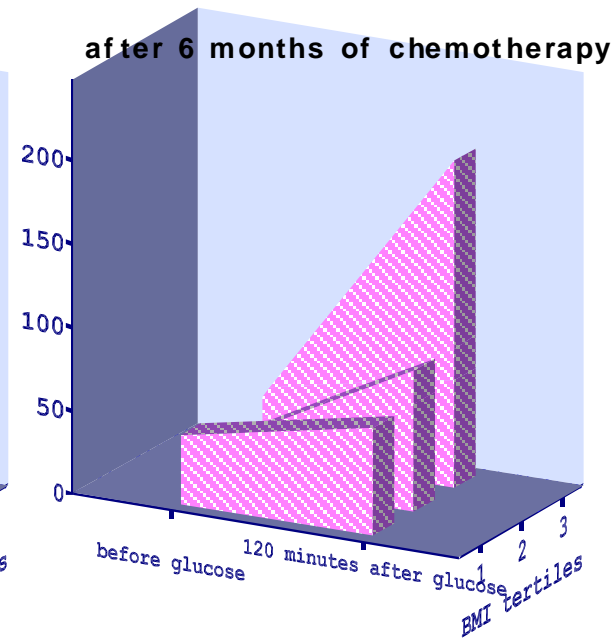
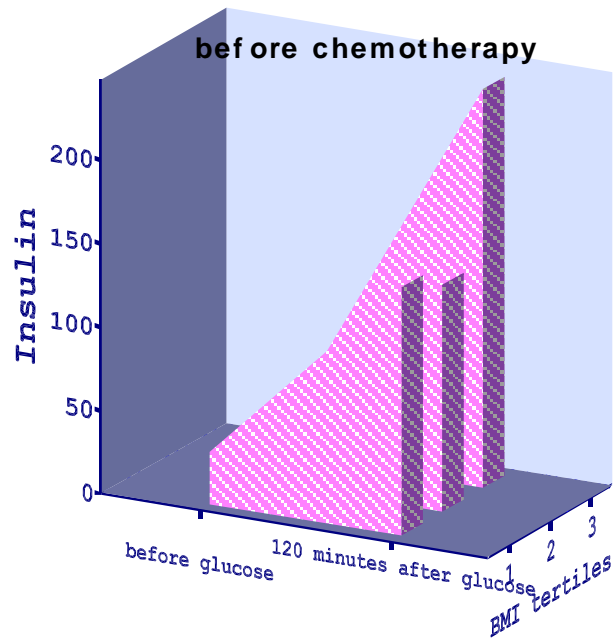
**In patients, after 6 months of chemotherapy, insulin levels 120' were statistically lower ( $111.75 \pm 76.19$  vs.  $170.39 \pm 78.07$  mU/ml,  $p=0.037$ ), while no difference was noticed in insulin levels 0'.**



**In patients, neither time 0', nor time 120' IL-1 levels differed significantly before and after successful chemotherapy.**

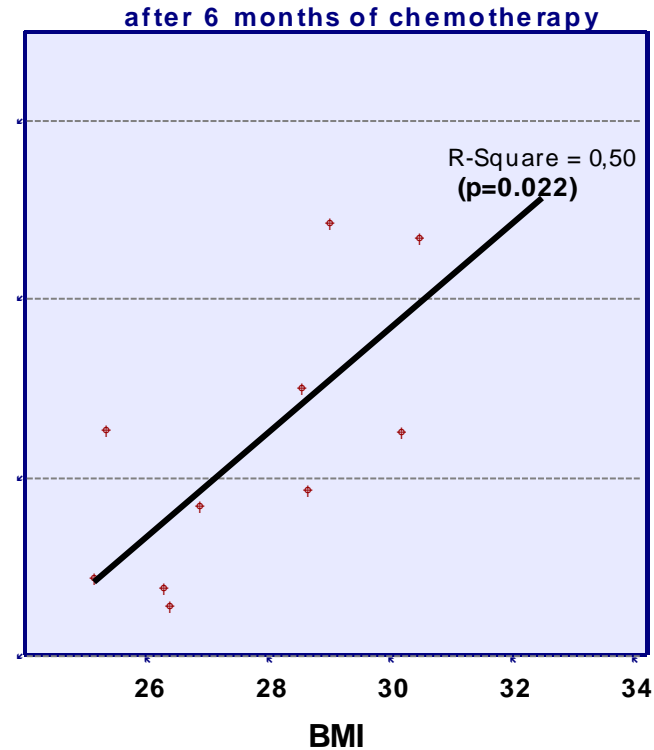
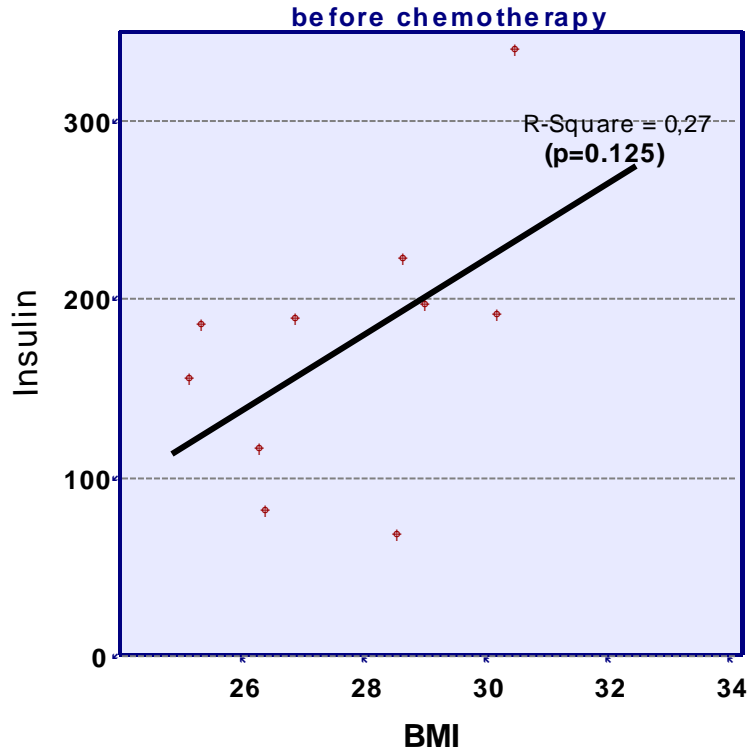


**In patients, neither time 0', nor time 120' IL-6 levels differed significantly before and after successful chemotherapy.**



**Area under the curve of insulin according to different BMI tertiles, before and after six months of chemotherapy**

# Insulin response to OGTT and BMI: a) before and b) after chemotherapy



## Multiple regression:

(R square=69.8, F=5.385, Sig=0.031)

Beta for BMI=0.364, p=0.180,

Beta for IL-8=1.097, p=0.005,

Beta for IGF-1=0.757, p=0.039

## Multiple regression:

(R square=90.2, F=11.44, Sig=0.010)

Beta for BMI=0.578, p=0.011,

Beta for IL-8=0.567, p=0.017,

Beta for age= -0.532, p=0.035,

Beta for TNF- $\alpha$ = -0.611, p=0.016

## Conclusions:

**Successful chemotherapy**

- a) results in lower post-prandial insulin levels, indicating that the effect of malignancy to insulin resistance is blunted and**
- b) at the same time reveals the well-known positive relationship between BMI and insulin resistance.**

