Background:
Sclerostin (SC), secreted by osteocytes, inhibiting Wnt canonical pathway in osteoblast, is responsible for reduced bone formation (1). SC serum levels are increased in patients affected by Chronic Kidney Disease (CKD) being positive correlated with vascular calcification also in patients with atherosclerotic vascular disease mainly in type 2 Diabetes (T2D) patients (2).

Aims:
Primary aim was to investigate the SC expression in the atherosclerotic plaques of patients who underwent carotid endarterectomy. The secondary aims were to verify potential differences between T2D and non T2D patients in terms of SC expression and if there was a correlation between SC serum level and expression in the atherosclerotic plaques.

Methods:
This was a cross-sectional study involving 46 subjects (age = 71.1 ± 6.7 years, 36 men), 15 T2D patients (disease duration 7.2 ± 5.0 yrs), that underwent carotid endarterectomy in order to remove critical atherosclerotic plaques (>70%). We have excluded patients affected by Type 1 diabetes mellitus, autoimmune disease, osteoporosis, end stage renal disease, sclerostosis, hyperparathyroidism, cirrhosis, previous bone fractures. the plaques were collected, decalcified in osteodec and processed for paraffin embedding (figure 1). The presence of SC was detected by immunohistochemistry using SC monoclonal antibodies (figure 2-3).

Results:
SC expression was detected in all atherosclerotic plaques. SC was more significantly expressed in the media compared to the intima (p<0.0001) (figure 4). SC was also detected in the core, the shoulder and peri-calcification of the plaque; moreover, SC expression was significantly increased in the core compared to the shoulder of the plaque (moderate and diffuse levels in the core were increased compared to the shoulder, p<0.0001 – figure 5). Finally, SC was not observed in lymphocytes, but it was detected in the macrophages and VSMC. VSMC seemed to show increased SC expression compared to macrophages (moderate level in the VSMC was increased compared to macrophages p<0.0001). SC expression was detected in all patients irrespective of diabetes diagnosis. No correlation was observed between SC serum level and SC expression in the atherosclerotic plaques.

Discussion:
We found, for the first time, SC expression in the atherosclerotic plaque irrespective of the presence of T2D and of serum SC levels, in patients affected by severe vascular disease and without osteoporosis and CKD. Our findings seem to suggest that the SC was mainly secreted by VSMC in the tunica media and in the core of the plaque compared to the remaining segments. Further evaluations need to be performed in order to clarify if SC is produced in the plaque itself.