



## Diagnosis of rare inherited glyoxalate metabolic disorders through in-situ analysis of renal stones

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The primary hyperoxalurias type I - III constitute rare autosomal-recessive inherited disorders of the human glyoxylate metabolism. By mechanisms that are ill understood progressive nephrocalcinosis and recurrent urolithiasis (kidney stone formation) often starting in early childhood, along with their secondary complications results in loss of nephron mass which progresses to end-stage renal failure over time. In the most frequent form, end-stage renal failure (ESRF) is the rule and combined liver/kidney transplantation respectively pre-emptive liver transplantation are the only causative treatment today. Hence, this contributes significantly to healthcare costs and early diagnosis is extremely important for a positive outcome for the patient.

We are developing a stone-based diagnostic method by in-detail multi-methods investigation of the crystalline moiety in concert with urine and stone proteomics. Stone analysis will allow faster analysis at low-impact for the patients in the early stages of the disease. First results from combined spectroscopic (Raman, FTIR) and geochemical micro-analyses (Electron Microprobe and Laser Ablation ICP-MS) are presented here that show significant differences between stones from hyperoxaluria patients and those formed by patients without this disorder (idiopathic stones). Major differences exist in chemistry as well as in morphology and phase composition of the stones. Ca/P ratios and Mg contents differentiate between oxalate-stones from hyperoxaluria patients and idiopathic stones. Results show that also within the different subtypes of primary hyperoxaluria significant differences can be found in stone composition. These imply differences in stone formation which could be exploited for new therapeutic pathways. Furthermore, the results provide important feedback for suspected but yet unconfirmed cases of primary hyperoxaluria when used in concert with the genetic methods routinely applied.