HOLMIUM: YAG LITHOTRIPSY: EFFECT OF POWER SETTINGS AND ANTI-RETROPULSION DEVICES

Jason Sea, MD, Lee Jonat, MD, Jinze Qiu*, Ben Chew, MD, FRCPC, Kin Chan, Thomas Milner, MD, FRCPC,Joel Teichman, MD, FRCPC :Vancouver, BC
(Presentation to be made by Dr. Sea)

INTRODUCTION AND OBJECTIVES: We studied the relationship between holmium:YAG lithotripsy power settings and fragmentation, fragment size, and retropulsion, with and without anti-retropulsion devices.

METHODS: In vitro studies quantified total fragmentation (TF) and fragment size distribution for varied Ho:YAG power settings. All stones were exposed to 500 J total energy with a 365 μm fiber in water. Stones were ablated in a 8 mm diameter cylinder without and with stabilization (Accordion and BackStop devices). TF and % fragments > 1 mm were measured. Optical computed tomography (OCT) measured ablation craters for uric acid, struvite and calcium oxalate monohydrate stones. Pressure transients were measured by needle hydrophone. Accordion and BackStop devices were directly ablated with 100J total energy at various power settings to simulate operative error (surgical pass point).

RESULTS: Stabilization had an effect on retropulsion and TF (Table). For non-stabilized stones, increased pulse energy caused increased retropulsion and decreased TF. With anti-retropulsion devices, no retropulsion occurred; TF increased and fragment size both increased as pulse energy increased. OCT showed symmetric craters with regular contours (Figure). Crater size varied proportionally to pulse energy, $p<0.01$. Pressure transients increased as pulse energy increased, with typical peak transients of <10 bars at 0.5J, and 20-30 bars at 2.0J, $p<0.01$. With direct ablation, both Accordion and BackStop showed increased damage as pulse energy increased. Even at 2.0J pulse energy, they retained shape and function.

CONCLUSIONS: When a given amount of total energy is applied, retropulsion increases as pulse energy increases. Energy is wasted and lithotripsy is compromised. Low pulse energy (0.2J - 0.5J) produces minimal retropulsion and tiny fragments. High pulse energy (1.0J -2.0J) produces faster lithotripsy but larger fragments. Anti-retropulsion devices are useful when high pulse settings are applied. The ideal power setting depends on whether the urologist wants tiny debris or is willing to basket larger fragments; and whether an anti-retropulsion device is used. At all pulse settings, pressure transients remain low and ablation craters remain predictable consistent with photothermal mechanisms.
HO:YAG LITHOTRIPSY EFFICIENCY FROM 500 J TOTAL ENERGY

	0.2 J 10 Hz	0.2 J 40 Hz	0.5 J 10 Hz	0.5 J 40 Hz	1.0 J 10 Hz	2.0 J 10 Hz	p-value
TF (g) no device	11 ± 2	23 ± 5	40 ± 12	20 ± 6	52 ± 12	48 ± 9	<0.001
% > 1 mm, no device	0	0	22	5	4	1	0.02
Retropulsion (mm), no device	26 ± 6	22 ± 5	58 ± 15	63 ± 9	98 ± 15	152 ± 38	<0.0001
TF (g), PercSys	13 ± 5	29 ± 5	45 ± 10	50 ± 7	85 ± 34	141 ± 29	<0.0001
% > 1 mm, PercSys	0	0	10	15	37	36	<0.0001
TF (g), BackStop	25 ± 1	21 ± 3	36 ± 8	47 ± 11	111 ± 37	140 ± 54	<0.0001
% > 1 mm, BackStop	0	3	0	27	38	41	<0.0001

THE IMPACT OF STATINS ON NEPHROLITHIASIS: A TEN-YEAR REVIEW OF AN EQUAL ACCESS HEALTH CARE SYSTEM

James H. Masterson, M.D., Roger L. Sur, M.D., Kerrin L. Palazzi-Churas, M.P.H., James O. L'Esperance, M.D., Brian K. Auge, M.D., Marshall L. Stoller, M.D.: San Diego, CA
(Presentation to be made by Dr. Masterson)

Background: The pathogenesis of urinary stone formation has not been completely elucidated. Traditional theories of abnormal urine chemistries do not fully explain urinary stone disease. Recently, vascular disease, hypertension, and obesity have been associated with nephrolithiasis. The purpose of this study was to investigate the relationship between hyperlipidemia and nephrolithiasis as well as the impact of statin medications on urinary stone formation.

Method: Patient medical records from Armed Forces Health Longitudinal Technology Application (AHLTA) of the Southwestern United States region was queried (January 2000 – October 2010) to identify adult patients with hyperlipidemia. AHLTA database is an electronic medical record for all active duty members, dependents and retirees. We created two predictor variables -- with and without anti-hyperlipidemic drugs—with the outcome variable as urinary stones; all subjects with a diagnosis of nephrolithiasis were identified as well. Descriptive and inferential statistics were performed.

Results: There were 57,326 subjects (63.8% male) with hyperlipidemia with a mean age 53 (SD+/- 16) years. Females were significantly older than males, 56 years (SD+/-16,) vs 51 years (SD+/-16) $p<0.001$. Of these subjects 1,998 subjects (3.5%) had a history of nephrolithiasis. During this time period there were a total of 6,313 subjects (61.7% male) with nephrolithiasis identified. In univariate analysis, statin medications reduced the risk of nephrolithiasis (OR=0.813, 95% CI 0.74-0.89, $p<0.001$). In univariate analysis, this reduction was significant for females (OR=0.6, 95% CI 0.51-0.70, $p<0.001$) but not males (OR=0.96, 95% CI 0.86-1.07, $p=0.418$). In multivariate analysis, the use of statin medications remained protective against stone formation (OR 0.506 95% CI 0.457-0.562, $p<0.001$), even when adjusting for age, sex, obesity, hypertension, diabetes, heart disease and arterial disease.

Conclusions: Hyperlipidemia appears to be related to nephrolithiasis, particularly significant for females. This is the first study to demonstrate the impact of statins on nephrolithiasis and supports further investigation into the vascular etiology of urinary stone formation.

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UNDERSTANDING OXALATE METABOLISM AND THE ROLE OF OXALOBACTER FORMIGENES AS A POSSIBLE TREATMENT

Chelsea N. Elwood*, MD, Marshall Stoller, MD, Ben H. Chew, MD & Dirk Lange*, Ph.D: Vancouver, BC, Canada
(Presentation to be made by Dr. Lange)

Introduction: Oxalate metabolism in the intestine plays an important role in hyperoxaluria and calcium oxalate urolithiasis. *Oxalobacter formigenes* decreases urinary oxalate levels, however the specific mechanisms are not understood.

Purpose: To understand the mechanisms linking oxalate absorption and degradation.

Materials and Methods: The capacity of rat intestinal segments to absorb oxalate (4 uM 14C-oxalate) were determined using Ussing Chambers. *O. formigenes* and colonic epithelial cell interaction was determined by *in vitro* tissue culture models and fluorescence microscopy.

Results: The jejunum had the highest capacity to absorb oxalate. Oxalate was absorbed along the entire length of the intestine but peaked in the jejunum. Adding 14C-oxalate on the serosal side of intestinal epithelial cell (CaCO2) monolayers and exposing the mucosa to *O. formigenes* lysates and whole cells, increased reverse transport of oxalate from the serosal to mucosal side. To better understand this interaction, we identified a bacterial surface
carbohydrate (lipooligosaccharde) used to serotype other bacteria. The structure of this carbohydrate differs between *O. formigenes* isolates.

Conclusions: We have shown that the capacity to absorb oxalate is highest in the jejunum (a sterile area), and that *O. formigenes* lysates and whole cells trigger oxalate secretion across colonic epithelial cells. We propose a mechanism that involves the interplay between jejunal and colonic events that lead to the overall decrease in urinary oxalate. In addition, we propose a target for a serotyping method that will allow for the study of strains, to identify the best colonizers, and to reduce gastrointestinal oxalate absorption.

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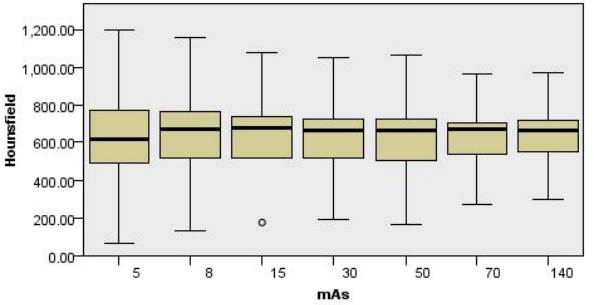
COMPARING STONE ATTENUATION IN LOW-DOSE AND CONVENTIONAL NONCONTRAST COMPUTERIZED TOMOGRAPHY

Damien L. Smith, MD, Jonathan P. Heldt*, BS, Gideon D. Richards, MD, Gautum Agarwal, MD, D. Duane Baldwin, MD: Loma Linda, CA
(Presentation to be made by Dr. Smith)

Background: Noncontrast computerized tomography (NCCT) is the radiographic modality of choice for stones due to its rapid and accurate image acquisition. In addition CT provides the Hounsfield Unit (HU) determination to assist in identifying stone type. Due to recent concerns about the high radiation exposure provided by conventional CT scans, many centers are developing low dose CT (LDCT) stone protocols. Although these protocols have been shown to detect stones with high sensitivity and specificity, it is not known whether these protocols are equally effective in determining the HU stone density. The purpose of this study is to determine if there is a difference in attenuation measurements when comparing low-dose radiation and conventional CT scans.

Materials and Methods: In this prospective randomized study 3 human cadavers were used to place 7 mm calcium oxalate stones into random locations in the proximal, mid and distal ureter. NCCT was performed for each stone configuration using different mAs radiation settings ranging from 5 to 140 mAs. Scans were read by a blinded urologist on an Impax workstation with images magnified to 4.0. The average attenuation of the voxels within a 4 mm ellipse that was entirely placed within each stone at its center was measured to determine the stone density. Identical measurements were performed in each stone at each of the 7 tested mAs settings. Statistical analyses were performed using a Kruskal-Wallis test and a Friedman's Two-Way Analysis of Variance by Ranks, with $p<0.05$ considered significant.

Results: In 19 different stone configurations with 133 stones, median attenuation levels of the observed stones were 614 HU at 5 mAs, 674 HU at 7.5 mAs, 681 HU at 15 mAs, 669 HU at 30 mAs, 670 HU at 50 mAs, 674 HU at 70 mAs, and 667 HU at 140 mAs. The differences in median attenuation levels were not significantly ($p=0.998$) different from each other at the different radiation settings (see graph). An increasing trend of attenuation variability was noticed as the radiation dosage decreased; however, this trend was not significant ($p = 0.411$).



Conclusion: When determining stone composition and density, measuring stone attenuation in LDCT is as reliable as measuring stone attenuation in conventional computerized tomography.

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IMPACT OF CALCIUM INTAKE AND INTESTINAL CALCIUM ABSORPTION ON KIDNEY STONES IN OLDER WOMEN: THE STUDY OF OSTEOPOROTIC FRACTURES (SOF)

Mathew D. Sorensen, MD, MS, Brian H. Eisner, MD, Katie L. Stone, PhD*, Arnold J Kahn PhD*, Li-Yung Lui, MA, MS*, Natalia Sadetsky, MD, PhD*, Marshall L. Stoller, MD: San Francisco, CA and Seattle, WA
(Presentation to be made by Dr. Mathew Sorensen)

Background: Intestinal calcium absorption is thought to play a critical role in nephrolithiasis; however, no study has directly assessed this association. The purpose of this study was to explore the relationship between radioactive intestinal calcium absorption, calcium intake, and nephrolithiasis.

Methods: The Study of Osteoporotic Fractures (SOF) is a prospective cohort of 9704 post-menopausal women recruited from population-based listings in 1986 and followed for more than 20 years. We performed secondary analyses of 7982 women, of which 5452 enrollees (82%) underwent oral radioactive calcium assay (^{45}Ca). The impact of dietary and supplemental calcium on intestinal fractional calcium absorption and the risk of nephrolithiasis were evaluated. Factors independently associated with nephrolithiasis were determined.

Results: Fractional calcium absorption decreased with increased calcium intake, with no difference between dietary and supplemental calcium. Fractional calcium absorption was higher in women with nephrolithiasis among all calcium intake groups. Increased dietary calcium intake reduced the likelihood of nephrolithiasis by 45-54% ($p=0.03$). Women with a history of kidney stones were less likely to supplement calcium ($p<0.001$). In adjusted analyses, calcium supplementation was associated with a 21-38% decreased likelihood of kidney stones ($p=0.007$). There was a 24% increased risk of kidney stones for each 10% increase in fractional calcium absorption ($p=0.008$) after adjustment. Elevated BMI was independently associated with a 70-82% increased risk of nephrolithiasis.

Conclusions: Intestinal calcium absorption plays an important role in the development of nephrolithiasis. Increased intestinal fractional calcium absorption is associated with an increased likelihood of nephrolithiasis. Fractional calcium absorption is higher in women with a history of kidney stones. Dietary and supplemental calcium decrease fractional calcium absorption and may protect against nephrolithiasis.

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