

A review of urinary stone analysis techniques

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ABSTRACT

Knowledge of the chemical composition and structure of urinary stones is of great value in the choice of treatment and prevention of recurrence. This is a brief review and a comparative study of the principles and practical application of various chemical and physical techniques used for urinary stone analysis. The different methods of classifying and grouping urinary stones by results of chemical analytic techniques are, also, compared and evaluated. In addition to reviewing various techniques used for the in-vitro analysis of removed stone samples, the newly emerging physical and radiological techniques for the in-vivo intact-stone analysis are, also, evaluated. These in-vivo techniques, particularly the rapidly advancing unenhanced spiral CT scanning, represent an important step forward towards the notion of non-destructive analysis of urinary stones while still in situ before the choice of treatment modality.

Saudi Med J 2006; Vol. 27 (10): 1462-1467

Urolithiasis is a multi-factorial recurrent rapidly increasing problem of universal distribution that causes substantial morbidity. Therefore, it is commonly believed that biochemical studies alone are never complete but correlation of clinical and biochemical results with that of chemical composition and structure of the stones is of great value in the delineation of pathogenesis, clinical management, preventive measures and choice of treatment modality. Until the late eighties, urinary stone analysis relied more on chemical rather than physical analytic techniques. The latter were considered not optimum for the quantitative analysis^{1,2} as it detects the constituent salts providing it is not less than 5% of the sample.^{1,3}

Chemical analytic techniques and classification of stones. The chemical analytic techniques detect the individual ions.^{1,4} In urinary stone analysis, the hospital laboratories relied only on the simple qualitative and semi-quantitative chemical analytic techniques⁵ which only give arbitrary information on stone composition.^{6,7} However, many investigators

appreciated the value of quantitative chemical analytic techniques and several schemes for the classification of urinary stones were suggested.^{5,8-13} Almost all the investigators utilized the resulting percentage composition of the constituting ions in considerable calculations based on certain assumptions to arrive at estimates for compounds.^{2,11,14-17} Hence, the comparison between these classifications is difficult as the findings of chemical analysis in each were presented in a different manner and neglecting minor components (10 or 20%) was a common practice in all of them. However, a simpler classification of urinary stones based only on the percentage composition of the constituting ions was offered.¹⁸ It successfully encompassed all the stone samples subjected to wet chemical analysis and also considered all the ions present whether trace (<2%) or minimum (2-10%) amounts; hence, the various stone groups were specified with precision. In approval of this classification, the results of microanalytic technique for the determination of total carbon, hydrogen and nitrogen confirmed the previous classification

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of the stone types and categories.¹⁸ In addition, the classification of 214 urinary stones using the cluster analysis technique of the results of their ex-vivo computerized tomographic (CT) scanning and chemical analysis¹⁹ was generally supportive to the previous classification and to the variables used for classifying the various stone groups.

Ionic correlations within urinary stones. Meanwhile, in some large lamellate urinary stones when the previous classification was applied on the chemical composition of various stone lamellae the subsequently identified groups and their lamellar arrangement pointed out to some ionic correlations which may help in predicting the stone type in recurrent stone formers.²⁰ On the other hand, in urinary stone analysis although different analytic techniques (chemical and physical) were used, they shared some similar information on the stone composition as the identification of 5 groups in the phosphate stones^{18,21} and the presence of <2% phosphate in uric acid stones^{2,11,18,22-24} also the presence of uric acid (<20%)^{11,18,23} and calcium phosphate^{2,11,15,18,22,23,25-28} in oxalate stones and 2-10% of uric acid in calcium phosphate ones,^{11,18} furthermore, infection stones are not oxalate but phosphate or uric acid^{11,18,29} and the latter is of very low relative frequency percentage.^{7,15,18,30} Meanwhile the infection phosphate stones are never pure struvite^{18,21,29,31-33} as it contains variable amounts of calcium oxalate^{2,18,31,32,34} or more frequently calcium phosphate.^{2,11,15,18,21,26,27-29,32,35-37}

Physical analytic techniques. On the contrary, for urinary stone analysis in the nineties, there was progressive increase in the use of physical techniques (infrared spectroscopy and x-ray diffraction photography) with decrease in relying on chemical methods which by now are considered to be obsolete.^{38,39} This is expected to add more to the ease of procedures, revealing more detailed information on fine cellular structure and possibly diagnosing the stone type in-vivo especially after the recent advances in these techniques. The x-ray diffraction photography and crystallographic techniques of polarization microscopy are useful tools in the study of the crystalline structure, order of deposition of components and the nucleus.⁴⁰⁻⁴⁵ However, as they need high technical skill and patience,^{15,21,25,26,46,47} x-ray diffraction photography is only employed now, in a small number (5-9%) of specialized laboratories.³⁹ In addition, electron probe analysis and scanning electron microscopy are useful too for the study of different crystalline forms and organic matrix as well.^{42,48-55} Accordingly, close examination of the urinary stones by scanning electron microscopy and similar high quality

sensitive analytic techniques as atomic absorption spectrophotometry,^{18,56,57} inductivity coupled plasma atomic emission spectroscopy,^{18,58,59} instrumental neutron activation analysis (INAA),⁶⁰ proton induced characteristic x-ray emission spectroscopy (PIXE)^{61,62} and nuclear reaction analysis (NRA)⁶² revealed several unexpected elements and trace elements mostly in the nuclear region of the stones such as Calcium, Magnesium, Sodium, Potassium, Copper, Aluminum, Zink, Iron, Phosphorus, Silicon, Cobalt, Chlorine, Lead, Titanium, Selenium, Strontium, Boron, Tungsten, Zirconium and Uranium. However, their role in the nucleation process of stone formation is still controversial as it is supported by some investigators^{18,60-62} and denied by others.⁵⁸ Meanwhile, all the previously used techniques are too cumbersome for routine purpose as they need special expertise and laborious sample preparation.⁷ However, there is a progressive increase in the use of infrared spectroscopy technique in various biochemical laboratories^{38,39} as it defines the stone composition with precision.^{18,43,63-68} Meanwhile, the new technique of near-infrared reflectance spectroscopy when compared to the infrared spectroscopy is simpler and identifies, with sufficient accuracy qualitatively and semi-quantitatively, mixed urinary stones with 2 or 3 components in short time even when the stone powder is <100 micrograms.⁶⁹ But, the modern Fourier transform infrared spectrophotometry (FT-IR) is the most advanced technique. It allows the identification of calculi components by detailed comparison with libraries of reference spectra.⁷⁰ Its application pointed out to the presence of false calculi or artifacts and calculi containing drugs, metabolites or usual components around unusual nucleus. Hence, it was recommended that analysis of all calculi should be a strategy as sometimes it gives a clue to the pathogenesis. Meanwhile, for the characterization of the 2 hydrates of the calcium oxalate salt (mono- and dihydrate), thermogravimetry (TG) technique and differential thermal analysis (DTA) were considered as the best physical methods.⁷¹ Hence, it was believed that TG method^{47,72-74} may inform us about the age of the stone^{72,73} and activity of the disease.⁷⁵ Furthermore, the simultaneous thermal analysis method TG-DTA would be an alternative method to the use of x-ray diffraction or Fourier transform infrared techniques for the quantitative determination of each hydrate of the calcium oxalate when present together in the presence of uric acid or magnesium ammonium phosphate.⁷¹ Moreover, in urinary stone analysis testing the usefulness of dual energy radiographic densitometry and solid-state nuclear magnetic resonance spectroscopy (NMR) showed

that the former technique⁷⁶ is of a little value in determining the stone composition though providing information on the mineral and non-mineral phases of the calculus. However, the latter technique^{70,77} detects and quantifies calcium oxalate, uric acid, struvite with calcium phosphate that closely resemble brushite and calcium hydroxy apatite (HA). Hence, it represents a new applicable technique.

In-vivo intact-stone analytic techniques.

Furthermore, the exposure of the stone to a pulsed dye laser beam resulted in a fluorescent emission which appeared to be especially related to the stone composition previously determined by x-ray diffraction. Thus, it is another new technique which may have a practical in-vivo application.⁷⁸ Generally, in urolithiasis, the advent of the non-invasive techniques of ultrasound and CT provided an advance especially in demonstrating non-opaque urinary calculi which may be uric acid, urates, xanthine, cystine or poorly mineralized matrix and differentiating them from blood clots and tumors.⁷⁹⁻⁸¹

In CT, it was found that in measurable non opaque calculi ($\geq 2\text{mm}$) no difference in the attenuation value in vivo or in vitro and no correlation between stone size and density.⁸² Meanwhile, sequential CT study is useful in the assessment of the position of the small calculi pre- and postoperatively especially in horseshoe or crossed fused ectopia where external and internal architectures are distorted. Also, it is useful in the dissolution therapy to determine its response^{83,84} although a small uric acid stone below the detection threshold size ($1.3\text{ mm} + 0.1$) is imperceptible even with the unenhanced helical CT,⁸⁵ which has evolved to a well accepted alternative to intravenous urography.⁸⁶ In addition, CT and the more advanced unenhanced helical CT may be adjunct to the laboratory methods for the differentiation among various types of renal calculi. In vitro, by using CT, differentiation between uric acid, struvite and calcium oxalate stones with overall accuracy of 89% was possible by the mean pixel value and standard deviation of the stones pixel value.^{87,88} However, the mean, maximum and modal pixel densities showed heterogeneity in the stone density and the uric acid stones were a distinct group. Also, the cystine stones were differentiated from struvite, calcium oxalate and brushite stones with 70% accuracy. However, calcium containing stones of various composition and struvite were not distinguished reliably.⁸⁹ Hence, better differentiation between various stone types was achieved on the basis of 3 parameters of CT data namely absolute CT values, dual CT values and pixel pattern. Thus, uric acid and cystine stones were significantly differentiated from the other types

($p < 0.001$). The struvite stones with low or moderate calcium phosphate were identified correctly with 80% accuracy. However, the following stones calcium oxalate, calcium phosphate and struvite with high calcium phosphate could not be differentiated from each other.⁹⁰ Meanwhile in vivo, using the advanced unenhanced helical CT showed significant difference ($p = 0.0367$) between the Hounsfield unit (HU) of the calculi predominantly composed of uric acid and that of the calculi predominantly composed of calcium oxalate.⁹¹ Furthermore, no significant difference was noted between the Hounsfield unit values of calcium oxalate and calcium phosphate; hence, they were considered collectively as calcium stones.⁹² However, significant difference ($p = 0.006$) was found between the mean HU density of calcium stones and uric acid stones. Also, the difference between the mean HU density of calcium stones and struvite stones was significant ($p = 0.073$). Otherwise, no significant differences were found among other stone types.⁹² Accordingly, as it was not possible to identify the various urinary stone types by either the mean HU values or HU density, a new technique was offered using more than one parameter of CT data namely absolute HU values, HU density, dual CT values⁹³ using a small collimation size.^{93,94} By the absolute HU values and HU density it was possible to differentiate with statistical significance between each of the following pure stone types uric acid (UA), calcium oxalate monohydrate (COM) and struvite in addition to their differentiation from most of the following mixed stones; COM 60-90% + hydroxyapatite (HA), COM 40-90% + UA, UA + COM <40% and struvite + COM + HA. Thus, differentiation with statistical significance was possible between pure UA and all mixed stone types except UA + COM <40% also between pure COM and mixed UA + COM <40%; and also pure struvite from all mixed stone types except mixed struvite stones. On the other hand, the dual CT values were not as good as the absolute HU values and HU density in the determination of stone composition on the basis of single CT evaluation. Furthermore, during spiral CT examination the recent advances in hardware and software technology enabled 3 dimensional figures of urinary stones. Hence, subsequent determination of linear dimensions along 3 coordinate axes and volumetric analysis of the calculi with high degree of accuracy becomes possible.⁹⁵ Accordingly, in vitro using microcomputed tomography (microCT),⁹⁶ an excellent information of the surface and internal structural deposition pattern was available from high resolution 3 dimensional images of intact urinary stones. Furthermore, the following 6 minerals UA, COM, COD, cystine, struvite and HA, which may be present in pure or heterogenous urinary stones were

identified and they had non-overlapping ranges of micro attenuation values. Therefore, this technique represents an important step forward towards the notion of non-destructive stone analysis in patients by the helical CT before the choice of treatment modality. In addition, another novel technique for intact stone analysis is the x-ray coherent scatter analysis using monoenergetic x-ray from the standard diagnostic x-ray equipment. As the coherent scatter properties depend on the molecular structure of the scattering media each of the stone components; COM, cystine, Magnesium ammonium phosphate and calcium phosphate demonstrated a distinct coherent scatter pattern which matches that of a pure chemical sample.⁶⁸ However, instead of monoenergetic x-ray, when using polyenergetic x-ray from the diagnostic x-ray equipment,⁹⁷ the coherent scatter analysis becomes as sensitive to stone component structure as the monoenergetic x-ray diffraction analysis. Therefore, it can be used in classifying urinary calculi by composition as it can detect the multiple stone components and show its structural arrangement.⁹⁷ Hence, with the use of appropriate collimation size, coherent scatter analysis may represent another technique for intact stone analysis in patients.

On the other hand, the relatively new technique of fiberoptic infrared spectroscopy⁹⁸ represents a new trend in urolithiasis. It is an alternative method to stone analysis especially after the use of Extra Corporeal Shock Wave Lithotripsy (ESWL), the best treatment choice, as the stone is fragmented into small particles. Therefore, the fiberoptic infrared spectroscopy technique is designed to detect qualitatively and quantitatively the various urinary salts present in fresh urine sample (without processing) with an average error of 20%.⁹⁸ However, further clinical research on this technique is essential to evaluate its potential.

References

1. Uldall A. Analysis of urinary calculi: A quality control programme. *Scand J Clin Lab Invest* 1981; 41: 339-345.
2. Sutor DJ, Wooley SE, Illingworth JJ. A geographical and historical survey of the composition of urinary stones. *Brit J Urol* 1974; 46: 393-407.
3. Sutor DJ, Wooley SE, Mackenzie KR, Wilson R, Scott R, Morgan HG. Urinary tract calculi - A comparison of chemical and crystallographic analyses. *Brit J Urol* 1971; 43: 149-153.
4. Uldall A. A wet chemistry method for the analysis of urinary calculi. *Scand J Clin Lab Invest* 1983; 43: 727-733.
5. Rose GA. Stone analysis by wet chemistry. In: Rose GA, editor. *Urinary Stones: Clinical and laboratory aspects*. Lancaster: MTP Press; 1982. p. 67-75.
6. Larsson L, Sorbo B, Tiselius HG, Ohman O. On the analysis of urinary calculi. In: Brockis JG, Finlayson B, editors. *Urinary calculus*. International Urinary Stone Conference. Littleton (MA): PSG Publishing Company; 1981. p. 383-386.
7. Otnes B. Urinary stone analysis, methods, materials and value. *Scand J Urol Nephrol Suppl* 1983; 71: 1-109.
8. Hodgkinson A. A combined qualitative and quantitative procedure for the chemical analysis of urinary calculi. *J Clin Path* 1971; 24: 147-151.
9. Hodgkinson A. Composition of urinary tract calculi from some developing countries. *Urol Int* 1979; 34: 26-35.
10. Hodgkinson A, Williams A. An improved calorimetric procedure for urinary oxalate. *Clin Chem Acta* 1972; 36: 127.
11. Fuss M, Simon J, Verbeelen D, Weiser M, Van Ianduyt P, Elskens J. Chemical analysis of renal stones from 377 Belgian patients by using qualitative or quantitative methods. *Eur Urol* 1978; 4: 90-93.
12. Farrington CJ, Liddy ML, Chalmers AC. A simplified sensitive method for the analysis of renal calculi. *Am J Clin Path* 1980; 73: 96-99.
13. Larsson L, Sorbo B, Tiselius HG, Ohman S. A method for quantitative wet chemical analysis of urinary calculi. *Clin Chim Acta* 1984; 140: 9-20.
14. Westbury EJ. Some observations on the quantitative analysis of over 1000 calculi. *Brit J Urol* 1974; 46: 215.
15. Sutor DJ, Wooley SE. Composition of urinary calculi by X-ray diffraction. Collected data from various localities. Parts XV-XVII. *Brit J Urol* 1974; 46: 229-232.
16. Sutor DJ, Wooley SE, Illingworth JJ. Some aspects of the adult urinary stone problem in Great Britain and Northern Ireland. *Brit J Urol* 1974; 46: 275-288.
17. Takasaki E. An observation on the composition and recurrence of urinary calculi. *Urol Int* 1975; 30: 228.
18. Abdel-Halim RE, Baghlaif AO, Sibaa AI, Merzibani M, Hadramy MS, Noorwali AA, et al. Urolithiasis in the western region of Saudi Arabia: A clinical, biochemical and epidemiological study. Urolithiasis in the western region of Saudi Arabia: A clinical, biochemical and epidemiological study, Riyadh (KSA): King Abdul Aziz City for Science and Technology; 1996. p 224-275.
19. Abdel-Halim RE, Abdel-Aal RE. Classification of urinary stones by cluster analysis of ionic composition data. *Computer Methods and Programs in Biomedicine* 1999; 58: 69-81.
20. Abdel-Halim RE, Alsibaa A, Baghlaif AO. The structure of large lamellar urinary stones. A quantitative chemical analytic study applying a new classification scheme. *Scand J Urol Nephrol* 1993; 27: 337-341.
21. Ghori TAK, Nagpal KC, Ali SZ. X-ray diffraction study of urinary calculi from the Meerut region. *Indian J Med Res* 1982; 5: 894-898.
22. Prien EL. The Analysis of Urinary Calculi. *Urologic Clinics of North America* 1974; 1: 220-240.
23. Ibrahim A, Zein M, Beileil O. Uric acid lithiasis in the Sudan. *The Journal of Tropical Medicine and Hygiene* 1977; 80: 173-176.
24. Cifuentes JM, Pourmand G. Mineral Composition of 103 Stones from Iran. *Brit J Urol* 1980; 55: 465-468.
25. Sutor DJ, Wooley SE. Composition of urinary calculi by X-ray diffraction: Collected data from various localities. *Brit J Urol* 1971; 43: 268-272.
26. Sutor D, Wooley SE. Composition of urinary calculi by X-ray diffraction. *Brit J Urol* 1972; 44: 287-291.
27. Esho JO. Analysis of urinary calculi formed by Nigerians. *Eur Urol* 1978; 4: 288-291.
28. Kambal A, Abdel-Wahab EM, Khatlab AH. The Composition of Urinary Stones in the Sudan. *Brit J Urol* 1979; 51: 342-344.

29. Herring LC. Observations on the analysis of ten thousand urinary calculi. *J Urol* 1962; 88: 545.
30. Klohn M, Bolle JE, Reverdin NP, Susini A, Baud CA, Graber P. Ammonium Urate Urinary Stones. *Urol Res* 1986; 14: 315-318.
31. Rao MVR, Agarwal JS, Taneja OP. Studies in urolithiasis: II. X-ray Diffraction analysis of calculi from Delhi region. *Indian J Med Res* 1976; 64: 1.
32. Reveilland RJ, Daudon M. Struvite stones analysis by Infrared Spectrophotometry in adults and children. In: Schwille PO, Smith LH, Robertson WG, Vahlensieck W, editors. Urolithiasis and related clinical research. New York and London: Plenum Press; 1985. p. 723-726.
33. Boistelle R, Abbona F, Berland Y, Grand Vuillemin M, Olmer M. The crystallization of magnesium ammonium phosphate (struvite) in acidic sterile urine. In: Schwille PO, Smith LH, Robertson WG, Vahlensieck W, editors. Urolithiasis and related clinical research. New York and London: Plenum Press; 1985. p. 793-796.
34. Khaliq A, Ahmed J, Khalid N. Infrared Spectroscopic Studies of Renal Stones. *Brit J Urol* 1984; 56: 135-139.
35. Nickel JC, Olson M, McLean RJ, Grant SK, Costerton JW. An Ecological Study of Infected Urinary Stone Genesis in an Animal Model. *Brit J Urol* 1987; 59: 21-30.
36. He JY, Liu GD, Shen SJ. Composition and Structure of Infected Stones. In: Schwille PO, Smith LH, Robertson WG, Vahlensieck W, editors. Urolithiasis and related clinical research. New York and London: Plenum Press; 1985. p. 723-726.
37. Cox AJ, Harries JE, Hukins DWL, Kennedy AP, Sutton TM. Calcium phosphate in catheter encrustation. *Brit J Urol* 1987; 59: 159-163.
38. Blijenberg BG, Baadenhuijsen H. Results of various analysis techniques in relation to urinary calculi studies. *Ned Tijdschr Geneesk* 1990; 29: 1402-1404.
39. Hesse A, Kruse R, Geilenkeuser WJ, Schmidt M. Quality control in urinary stone analysis: results of 44 ring trials (1980-2001). *Clin Chem Lab Med* 2005; 43: 298-303.
40. Prien EL, Prien EJ Jr. Composition and structure of urinary stones. *Am J Med* 1968; 45: 654.
41. Schubert G, Brien G, Adam K. Studies on the occurrence of texture types in calcium oxalate urinary stones. *Z Urol Nephrol* 1990; 83: 373-381.
42. Leusmann DB, Blaschke R, Schmandt W. Results of 5035 stone analysis: A contribution to epidemiology of urinary stone disease. *Scand J Urol Nephrol* 1990; 24: 205-210.
43. Daudon M, Jungers P. Analytical methods of calculi and urinary crystals. *Rev Prat* 1991; 41: 2017-2022.
44. Quyang JM, Li XP. Combined analysis of urinary stones by x-ray photoelectron spectroscopy and x-ray powder diffraction. *Zhongguo Yi Xue Ke Xue Yuan Xue Bao* 2003; 25: 710-713
45. Ansari MS, Gupta NP, Hemal AK, Dogra PN, Seth A, Aron M, et al. Spectrum of stone composition: structural analysis of 1050 upper urinary tract calculi from northern India. *Int J Urol* 2005; 12: 12-16.
46. Gray D, Laing M. Powder diffraction analysis of urinary calculi: The advantages of using a cobalt X-ray tube. *J Urol* 1982; 127: 387.
47. Tozuka K, Konjiki T, Sudo T. Study of passed stones by means of X-rays, infrared and thermal analyses. *J Urol* 1983; 130: 1119-1122.
48. Khan SR, Hackett RL, Finlayson B, Konicek JR. Light and scanning electron microscopic studies of oxamide urolithiasis in rats. *Scan Electron Microsc* 1981; (Pt 3): 155-162.
49. Khan SR, Finlayson B, Hackett RL. Rat renal papillary structure in oxalate-induced microlithiasis, a scanning electron microscope study. In: Smith LH, Robertson WG, Finlayson B, editors. Urolithiasis: Clinical and basic research. New York: Plenum Publishing Corporation; 1981.
50. Khan SR, Finlayson B, Hackett RL. The ultra structure of rat renal tubules in experimental calcium oxalate nephrolithiasis. In: Smith LH, Robertson WG, Finlayson B, editors. Urolithiasis: Clinical and Basic Research: Plenum Publishing Corporation; 1981. p. 523.
51. Khan SR, Finlayson B, Hackett RL. Agar-embedded urinary stones: A technique useful for studying microscopic architecture. *J Urol* 1983; 130: 992.
52. Khan SR, Finlayson B, Hackett RL. Stone matrix as proteins absorbed on crystal surfaces: A microscopic study. *Scan Electron Microsc* 1983; (Pt 1): 379-385.
53. Khan SR, Hackett RL. Microstructure of decalcified human calcium oxalate urinary stones. *Scan Electron Microsc* 1984; (Pt 2): 935-941.
54. Khan SR, Hackett RL. Identification of urinary stone and sediment crystals by scanning electron microscopy and X-ray microanalysis. *J Urol* 1986; 135: 818-825.
55. Khan SR, Hackett RL. Histochemistry of colloidal iron stained crystal associated material in urinary stones and experimentally induced intrarenal deposits in rats. *Scan Electron Microsc* 1986; (Pt 2): 761-765.
56. Durak I, Yasar A, Yuratarslan Z, Akpoyraz M, Tasman S. Analysis of magnesium and trace elements in urinary calculi by atomic absorption spectro-photometry. *Brit J Urol* 1988; 62: 203-205.
57. Dawson JD, Heaton FW. Determination of magnesium in biological materials by atomic absorption spectrophotometry. *Biochem J* 1961; 80: 99.
58. Hofbauer J, Steffan I, Hobarth K, Vujcic G, Schwetz H, Reich G, et al. Trace elements and urinary stone formation: new aspects of the pathological mechanism of urinary stone formation. *J Urol* 1991; 145: 93-96.
59. Wandt MA, Underhill LG. Covariance biplot analysis of trace element concentrations in urinary stones. *Brit J Urol* 1988; 61: 474-481.
60. Lin SM, Tseng CL, Yang MH. Determination of major, minor and trace elements in urinary stones by neutron activation analysis. International Journal of Radiation Applications and Instrumentation Part A. *Applied Radiation and Isotopes* 1987; 38: 635-639.
61. McConville BE. Analysis of urinary calculi. *Journal of Radioanalytical Chemistry* 1982; 70: 21-28.
62. Saint A, Dyson NA. Nuclear techniques for the analysis of urinary calculi. *Brit J Urol* 1990; 66: 232-239.
63. Belcher DE. Analysis of renal calculi by infrared spectroscopy. *J Urol* 1955; 73: 653.
64. Tsay YC. Application of infrared spectroscopy to analysis of urinary calculi. *J Urol* 1961; 86: 838.
65. Sutor DJ, Scheidt S. Identification standards for human urinary calculus components, using crystallographic methods. *Brit J Urol* 1968; 40: 22-28.
66. Oliver LK, Sweet RV. A system of interpretation of infrared spectra of calculi for routine use in the clinical laboratory. *Clin Chim Acta* 1976; 72: 17-32.
67. Lafaut JP, Daudon M, Hardeman M, Werbrouck P. Composition of urinary calculi defined with precision by infrared spectrophotometry. *J Urol (Paris)* 1992; 98: 152-155.
68. Batchelar DL, Chun SS, Wollin TA, Tan JK, Beiko DT, Cunningham IA, et al. Predicting urinary stone composition using x-ray coherent scatter: a novel technique with potential clinical applications *J Urol* 2002; 168: 260-265.

69. Peuchant E, Heches X, Sess D, Clerc M. Discriminant analysis of urinary calculi by near-infrared reflectance spectroscopy. *Clin Chim Acta* 1992; 205: 19-30.
70. Sabot JF, Bornet CE, Favre S, Sabot-Gueriaux S. The analysis of peculiar urinary (and other) calculi: an endless source of challenge. *Clinica Chimica Acta* 1999; 283: 151-158.
71. Kaloustian J, El-Moselhy TF, Portugal H. Determination of calcium oxalate (mono and dehydrate) in mixtures with magnesium ammonium phosphate or uric acid: The use of simultaneous thermal analysis in urinary calculi. *Clin Chim Acta* 2003; 334: 117-129.
72. Strates B, Georgacopoulou C. Derivatographic thermal analysis of renal tract calculi. *Clin Chem* 1969; 15: 307.
73. Rose GA, Woodfine C. The thermogravimetric analysis of renal stones (in clinical practice). *Brit J Urol* 1976; 48: 403-412.
74. Rose GA. Stone analysis by thermogravimetric technique. In: *Urinary Stones: Chemical and laboratory aspects*. Lancaster: MTP Press; 1982. p. 77-85.
75. Koide T, Itatani H, Yoshioka T, Ito H, Namiki M, Nakano E, et al. Clinical manifestations of calcium oxalate monohydrate and dihydrate urolithiasis. *J Urol* 1982; 127: 1067-1069.
76. Burgos FJ, Minaya A, Saez JC, Sanchez J, Sanz J, Avila S, et al. The usefulness of dual-energy radiographic densitometry (Do) in establishing the composition of calculi. *Arch Esp Urol* 1993; 46: 392-398.
77. Bak M, Thomsen JK, Jakobsen HJ, Petersen SE, Petersen TE, Nielsen NC. Solid-state ¹³C and ³¹P NMR analysis of urinary stones. *J Urol* 2000; 164: 856-863.
78. Holden D, Whitehurst C, Rao PN, King TA, Blacklock NJ. Identification of urinary stone composition by pulsed dye laser. *Br J Urol* 1990; 65: 441-445.
79. Stiris MG. CT evaluation of non opaque renal calculus. *Scand J Urol Nephrol* 1981; 15: 341-342.
80. Federle MP, McAninch JW, Kaiser JA, Goodman PC, Roberts J, Mall JC. Computed tomography of urinary calculi. *AJR* 1981; 136: 255-258.
81. Borkowski GP, George CR, O'Donovan PB. Non urographic evaluation of renal calculous disease. *Cleveland Clinic Quarterly* 1985; 52: 3-9.
82. Parienty RA, Ducellier R, Pradel J, Lubrano JM, Coquille F, Richard F. Diagnostic value of CT numbers in pelvocaliceal filling defects. *Radiology* 1982; 145: 743-747.
83. Dunnick NR, Korobkin M. Computed tomography of the kidney. *Radiologic Clinics of North America* 1984; 22: 297-313.
84. Resnick MI, Kursh ED, Cohen AM. Use of computerized tomography in the delineation of uric acid calculi. *J Urol* 1984; 131: 9-10.
85. Tublin ME, Murphy ME, Delong DM, Tessler FN, Kliewer MA. Conspicuity of renal calculi at unenhanced CT: effects of calculus composition and size and CT Technique. *Radiology* 2002; 225: 91-96.
86. Pfister SA, Deckart A, Laschke S, Dellas S, Otto U, Buitrage C, et al. Unenhanced helical computed tomography vs intravenous urography in patients with acute flank pain: accuracy and economic impact in a randomized prospective trial. *Eur Radiol* 2003; 13: 2513-2520.
87. Hillman BJ, Drach GW, Tracey P, Gaines JA. Computed tomographic analysis of renal calculi. *AJR* 1984; 142: 549-552.
88. Drach GW, Hillman BJ, Tracey P, Gaines JA. Computed tomographic analysis of the composition of renal calculi. In: Schwille PO, Lynwood HS, Robertson WG, Vahlensieck W, editors. *Urolithiasis and Related Clinical Research* Edited. New York, London: Plenum Publishing Corporation; 1985. p. 743-746.
89. Newhouse JH, Prien EL, Amis Jr ES, Dretler SP, Pfister RC. Computed tomographic analysis of urinary calculi. *AJR* 1984; 142: 545-548.
90. Mitcheson HD, Zamenhof RG, Bankoff MS, Prien EL. Determination of the chemical composition of urinary calculi by computerized tomography. *J Urol* 1983; 130: 814-819.
91. Sherwin A, Douglas HG, Myron P, Donna B, Stephen NY. Determination of stone composition by non contrast spiral computed tomography in the clinical setting. *J Urol* 1999; 161: 366.
92. Motley G, Dalrymple N, Keesling C, Fischer J, Harmon W. Hounsfield unit density in the determination of urinary stone composition. *Urology* 2001; 58: 170-173.
93. Sheir KZ, Mansour O, Madbouly K, Elsobky E, Abdel-Khalek M. Determination of the chemical composition of urinary calculi by non contrast spiral computerized tomography. *Urol Res* 2005; 33: 99-104.
94. Saw KC, McAteer JA, Monga AG, Chua GT, Lingeman JE, Williams JC Jr. Helical CT of urinary calculi: effect of stone composition, stone size, and scan collimation. *AJR Am J Roentgenol* 2000; 175: 329-332.
95. Olcott ED, Sommer FG. Unenhanced CT in the evaluation of urinary calculi: application of advanced computer methods. *Semin Ultrasound CTMR* 1999; 20: 136-141.
96. Zarse CA, McAteer J, Sommer AJ, Kim SC, Lingeman EJE, Evan AP, et al. Nondestructive analysis of urinary calculi using micro-computed tomography. *BMC Urol* 2004; 4: 15-26. (Available from URL: <http://www.biomedcentral.com/1471-2490/4/15> and at: <http://www.pubmedcentral.gov/articlerender.fcgi?tool=pubmed&pubmedid=15596006>).
97. Davidson MT, Batchelar DL, Velupillai S, Denstedt JD, Cunningham IA. Analysis of urinary stone components by x-ray coherent scatter: characterizing composition beyond laboratory x-ray diffractometry. *Phys Med Biol* 2005; 50: 3773-3786. (Available from URL: <http://www.iop.org/EJ/abstract/0031-9155/50/16/008/>)
98. Cytron S, Kravchick S, Sela BA, Shulzinger E, Vasserman I, Raichlin Y, et al. Fiberoptic infrared spectroscopy: A novel tool for the analysis of urine and urinary salts in situ and in real time. *Urology* 2003; 61: 231-235.