

ONE CENTURY OF URORADIOLOGY IN EUROPE: 1896 – 1996

Section 3: THE CHILDREN (1980-1989)

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“Reducing adverse side effects from the use of any new drug or technology must be our continued, collective goal.” Bruce McClennan, Hickey Lecturer, 1990 [1].

Major political and economic changes affecting Europe in the late twentieth century included globalisation of the economy, the success of the Asian economies and the fall of the Iron Curtain with the emergence of free Eastern European countries. Healthcare and radiology were constrained by strict budgetary control in most countries, at a time when new imaging technologies and digital imaging were developing rapidly. New diseases such as AIDS also put pressure on healthcare budgets.

TWOSTEPSFOREUROPEANRADIOLOGY ON THE WAY TO THE 21ST CENTURY.

International Congress of Radiology, ICR 1981, Brussels, Belgium. Belgian radiology took over leadership of European radiology from the Scandinavians in the early 1980s because the Belgian government took note of the *15th International Congress of Radiology* in 1981 in Brussels, under Professor Louis Jeanmart's presidency, and invested early in modern imaging technology. At ICR'81 the decline of conventional radiology and the boom of digital imaging became apparent. As in 1929, when the birth of IVU and angiography occurred during the worst economic crisis of the century, computed multi-modality medical imaging technology developed quickly despite the financial difficulties of the time. The introduction of computed tomography (CT) scanning coincided with the oil crisis and the development of magnetic resonance (MR) imaging with the Gulf War. Alan Davidson and André-Noël Dardenne featured the GU course program.

International Congress of Radiology, ICR 1989, Paris, France. At ICR'89, the radiological concept of subspecialisation by organ had to be revised because the new medical imaging technologies

depicted anatomical volumes. The conventional organ system based approach to analogic radiology was on the way to obsolescence [2]. Also, the new role and importance of interventional radiology was presented. Interestingly, an “*Endourology Society*” was created in the mid 1980s because of the development of many new interventional methods including extra-corporeal shock wave lithotripsy and many types of puncture and catheterisation of the organs and duct of the genito-urinary tract [3].

WHITHER EUROPEAN URORADIOLOGY ?

Genito-Uroradiology came of age when CT and US replaced conventional intravenous urography (IVU) and retrograde pyelography (RUP). This was less easy than might be imagined today because the budgetary constraints imposed by governments and administrations in Europe and Northern America prevented the rapid replacement of IVU by CT. Some GU radiologists, such as Michel and Moreau in Paris, unlike Annick Pinet in Lyon, Kasbarian in Marseille, Joffre in Toulouse, Jean Tavernier in Bordeaux, were frustrated by being unable to obtain CT then MR equipment for a number of years; Lemaître in Lille was happier because he could work with his closest Belgium colleagues. Similar delays occurred in Italy and the UK but not in Sweden and Germany. However, more and more GU subspecialists emerged because they dedicated a major part of their clinical activities and/or their research programs to CT and/or MR of the GU tract. This was particularly helpful to German radiologists who could escape the domination of the urologists in GU radiology. In Genito-Uroradiology, the volumetric approach helped to lead to more equal balance between the urinary tract and the genital tract. However, many GU radiologists were attracted by two other possibilities: joining the Abdominal Imaging



Fig. 1. Annick Pinet



Fig. 3. Judith A.W. Webb

Fig. 2. Ludovico Dalla Palma

Fig. 4. Henrik S. Thomsen



fraternity or becoming CT or MR specialists, like the angiographers of the 1960s and the US specialists of the 1970s. The changes caused difficulties for the Society of Uroradiology (SUR) in the USA [5]. In 1986, three past-presidents of the SUR, GW Hartman, McClennan and RC Pfister predicted that [6]: *«Radiologic education, research, and the practice of radiology will be of the highest quality in the future if academic departments stress organ-system subspecialization while continuing to integrate and interface with technique-based specialists¹. Planning should begin now to effect an orderly progression to an organ-system-based subspecialty structure for radiology training in general and for uroradiology specifically. Uroradiologists should remain as central consultants to their clinical counterparts, working collaboratively with urologists in clinical endeavors of mutual relevance. More fellowships in uroradiology should be offered that attempt to incorporate all imaging methods and procedures into the curriculum. These issues are addressed in the context of patient care, service, education, and cost containment.»*

In the USA, Bruce McClennan opened the way for CT to become a GU tool within the remit of the SUR with a paper in 1979 [7]. *«CT did take over all IVPs but not till the 90's really with spiral and MDCT»*, he wrote in a recent personal communication [8]. The SUR and the GU sessions at the RSNA Chicago meetings attracted more general or non-GU radiologists to present papers dedicated to GU topics, including interventional radiology.

More and more Europeans applied in the 1980-90s to be elected corresponding members of the SUR. Annick Pinet from France (Fig. 1), Marjorie Hertz from Israel, Leif Ekelund and Klaes Golman from Sweden, Ludovico Dalla Palma from Italy (Fig. 2), Judith Webb from the UK (Fig. 3), Henrik Thomsen from Denmark (Fig. 4), and François Cornud from France were among those who wanted to have the international GU label that only SUR membership could then give. The European members of SUR were aware of the problems of the SUR caused by the changes in the subspecialty and, when they created the *European Society of Uroradiology*² (ESUR) in the early 1990s, they were able to include practitioners of the new techniques in their subspecialty group.

1 In 1989, there were three subspecialist European organ radiology societies: *Cardiovascular and Interventional Radiological Society of Europe* (CIRSE), *European Society of Neuroradiology* (ESNR) and *European Society of Head and Neck Radiology* (ESHNR).

2 In 1998, ESUR changed its full title to *European Society of Urogenital Radiology*.

European radiology leaders, specifically Professors Albert L. Baert, Peter Josef Ell, Jacques Henry, Herwig Imhof, Josef Lissner [9] and Paul F.G.M. van Waes who was also an administrator of the ESNHR, **had already realised it was necessary to have a strong and credible *European Association of Radiology (EAR)*³ holding its own *European Congress of Radiology (ECR)*** [10].

European uroradiologists recognised the importance of following this trend [11]. Paul van Waes of Utrecht organised a successful SUR meeting in Scheveningen, Netherlands, in 1986. Then in 1987 Henrik Thomsen brought together the Northern European GU radiologists in Copenhagen for a first GU symposium, at which Latin Europeans were largely absent. Dalla Palma and Moreau and gave their full support to Thomsen's proposal for a *European Society of Uroradiology*. This made it possible to include the Latin Europeans in the group for the second GU symposium in Copenhagen in 1990.

CONTRAST MEDIA IN MEDICAL IMAGING, 1979-1989.

In the period 1950-1980, radiologists involved in contrast medium research were often those with a special interest in urinary tract imaging. This was because the iodinated contrast agents used were excreted by the kidneys and at that time intravenous urography was a common investigation. In the period 1980-1990, the involvement of GU radiologists in contrast media research continued. The 1980s saw the development in Europe of lower osmolality



Fig. 17. Jeffrey Newhouse and Bruce McClennan, SUR Gold Medallists. (Courtesy of Dr. McClennan).

3 The *European Society of Radiology* (ESR) replacing the *European Association of Radiology* (EAR) was founded in 2005..

iodinated agents (LOCM), suitable for intravascular administration. The new contrast media emerged into a market which until then had been dominated by the triiodinated hyperosmolar contrast media (HOCM). LOCM were associated with less side effects but they were expensive and their cost-effectiveness was difficult to assess. Side effects still occurred, mostly cardio-vascular collapse and anaphylactoid reactions such as angio-oedema (Quincke's edema) and very rarely sudden death, despite active resuscitation.

In his Hickey Lecture in 1990, McClennan stated [1]: *"The search for better radiopaque iodinated contrast material for intravascular use is continuing, but the recent development of new lower osmolality contrast media (LOCM), both ionic and nonionic, has dramatically affected the practice of radiology. The major issue retarding the introduction of LOCM into clinical practice in this country has been the increased cost of the media. Numerous preliminary assumptions and probabilities about the tolerance, efficacy, and overall safety of LOCM have been documented in scientific studies. The lower osmolality, reduced chemotoxicity, and high hydrophilicity of new compounds, particularly the nonionic variety compared with conventional high osmolality ionic agents (HOCM), offer a significant margin of safety to patients with known risk factors. Mounting data suggest that low or no risk patients are benefited as well, perhaps to an even greater degree. Costly trade-offs to the universal use of LOCM exist, therefore careful consideration of the advantages and disadvantages of LOCM for intravascular administration is required."*

Elliott C Lasser of San Diego was recognized as the leader of contrast media research by the international community at the International Congress of Radiology (ICR, Madrid, Spain) in 1973 (Fig. 10). He had been interested in the biological effects of techniques and contrast media used in radiology from the early 1950s [24,25]. He was the first radiologist to apply the advances in allerge-immunology to the study of the general toxicity of contrast media. Initially he studied the histamine-release effect [26,27] and then during 1980s he placed strong emphasis on the effects of contrast media on the activation of the complement system through Factor XII and bradykinin [28]. His aim was to find a way to reduce the incidence of adverse reactions to contrast media, which still had an associated mortality, albeit very low [29]. Lasser was Chairman of the Department of Radiology at the

University of California, San Diego (UCSD), and recruited many scientists to work on contrast media research [30]. Amongst them was Lee Talner, head of the GU section at UCSD until he moved to the University of Washington, Seattle, in 1994. Talner mentored some of the founding members of ESUR who worked with him at UCSD: Sven Dorph [34], Judith Webb [35] and Henrik Thomsen [36,37,38]. Talner often involved his European friends when he was looking for general consensus in problems in GU radiology [39,40]. Lasser's staff participated in the symposium on contrast media research held in May 1979 at Colorado Springs, Co, USA. The British nephrologist William Cattell [41] and JF Moreau [42] spoke at the GU session chaired by Lee Talner.

The other American team with an early interest in contrast media research was led by the GU radiologist Harry W Fischer of Rochester, New York (1921-1998) [43], who worked on uroangiographic contrast media [45,46]. His pupils, Richard Katzberg [47] and Robert Spataro (48), were both active SUR members.

Many European and American contrast medium researchers came together in September 1981 at a highly successful contrast medium symposium organised by Michel Amiel and Jean-François Moreau in Lyon. This drew attention of the North Americans to the active research being undertaken in Europe (49).

CONTRAST MEDIA RESEARCH SYMPOSIA (CMR)

Following the Lyon symposium, Amiel and Moreau invited Harold Baltaxe (†), Geoffrey Benness, Robert Brasch, Ronald Grainger (†), Charles Higgins and Elliott Lasser to discuss convening a meeting of the major scientific groups working on contrast media research every two years alternately in the USA and in Europe. The first Contrast Medium Research (CMR) symposium was co-chaired by Harry Fischer and Elliott Lasser in 1983 in San Francisco [50,51]. Moreau, working closely with Elliott Lasser, was elected convenor of the second symposium held in Montbazou, France, [52]. A third of the program was given to industry with four delegates who each gave three non peer reviewed papers. The two other thirds were selected from submitted abstracts and were subsequently published in Investigative Radiology. There were eighty participants from all over the world and the meeting was conducted in English. Benness and Fischer co-convened CMR'89 in Sydney, Australia [60].

STATISTICS

In the early 1980s only two teams were able to provide homogeneous statistics of contrast medium adverse events and morbidity from a single centre. Michel, in 1981, in Lyon, presented a series of 80,339 patients referred for an IVU at the Hôpital Necker in the period 1965-1981 [55]. The survey was retrospective and not randomized. The great majority of the IVUs were performed with injections of triiodinated hyperosmolar contrast media between 1965 and 1980, when LOCM were only available for research protocols. Michel observed anaphylactoid reactions in 44 cases [Table 1]. Of these, 35 occurred in the group of 57,846 non premedicated patients (1/1681 IVUs) with one death because of bronchospasm early in the study. There were nine reactions in the group of 21,493 patients (1/2388 IVUs) who had premedication with a steroid (dexamethasone, Soludécadron®) and an antifibrinolytic agent (ϵ -aminocaproic acid, Hemocaprol®, Capramol®).

The same year, Glen W Hartman *et al.* at Mayo Clinic, Rochester, Minnesota [56], reported an

impressive series of 300,000 consecutive patients with the following abstract: *"In a series of 300,000 consecutive patients who underwent excretory urography between January 1, 1964 and January 5, 1982, four deaths were recorded (a mortality rate of 1.3:100,000). All four patients who died were 50 years of age or older, all had a history of some type of hypersensitivity, all had a respiratory component to the reaction, all received a 1 ml test dose and had no reaction, and none had received a prior injection of contrast medium. The mortality rate in this series (1:75,000) is significantly lower than recently reported rates from multi-institutional studies and is similar to the mortality rate resulting from the parenteral administration of penicillin. Differences in reported series may relate to methods of data collection, variations in patient population, and therapeutic management."*

PATHOGENESIS

In his lecture at CMR'87, Moreau tried to amalgamate the different pathogenic theories of acute adverse reactions, including Lasser's complement-

CONTRAST MEDIA '87 World Symposium

Montbazou, France
May 25-29, 1987

Jean-Francois Moreau, MD
Chairman

Fig. 16

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▲ Fig. 15. JF Moreau and Elliott Lasser at Lee Talner's garden party. November 1980. (Courtesy of Dr. LB Talner).

Fig. 17. Participants-Attendees at Contrast Media Symposium CM'87, Montbazou, France. (Courtesy of Dr. Martii Kormanov)

▼ Elliott Lasser and Harry Fischer ▼



Factor XII activation and the role of C1-esterase inhibitor, Michel's controversial fibrinolytic effect and Lalli's vagal reaction to stress [57] [Fig. 21, 22 and 23]. At the same meeting, Katayama *et al.* [58] presented the preliminary results of the large Japanese survey, which conclusively showed the reduced incidence of side-effects with the new low osmolar nonionic contrast media [59] [Fig. 24].

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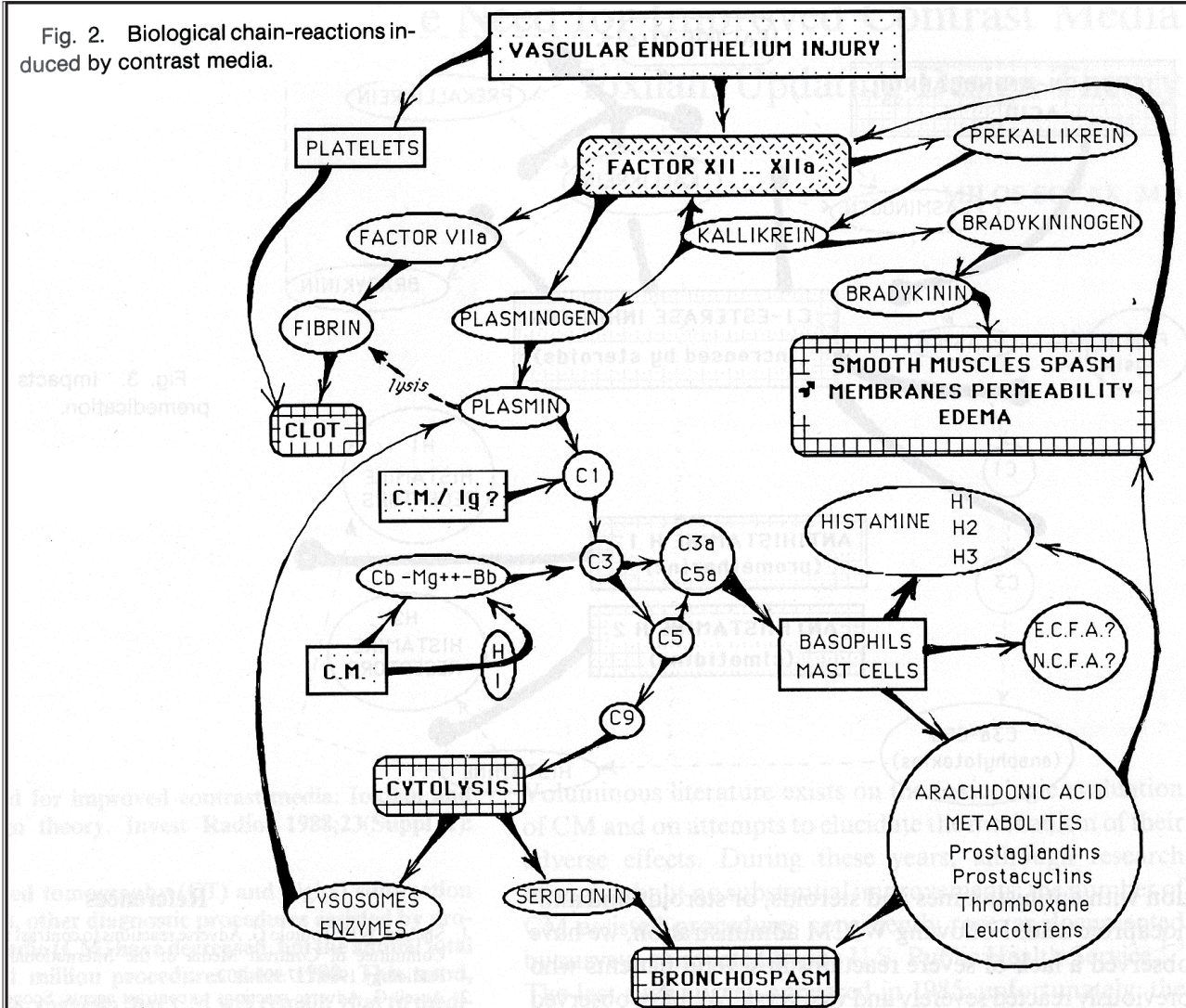
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		Non premedicated patients		Premedicated patients	
		1965-1978	1979-Jul 1981	1965-1978	1979-Jul 1981
IVU		58,846	0	8046	13,447
SHOCKS	mild	18		2	7
	moderate	9		0	0
	severe	8*		0	0
		(*1 death)			
Vagal reactions			23		62
urticaria-rash			155		123
Quincke edema			45		38
Spasmophilia			14		2
phlebitis			16		22

Table 1. IVU's statistics of mortality and morbidity at the Necker Hospital of Paris (1965 - Jul 1981)

Michel JR (1982) Prevention of shocks induced by intravenous urography. In: Amiel M (ed) *Radiological contrast media. Evaluation and future.* Springer Verlag, Berlin, Heidelberg, New York, 11- 13 [([]

Fig. 2. Biological chain-reactions induced by contrast media.



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Fig. 3. Impacts of drugs used for premedication.

CMR'87

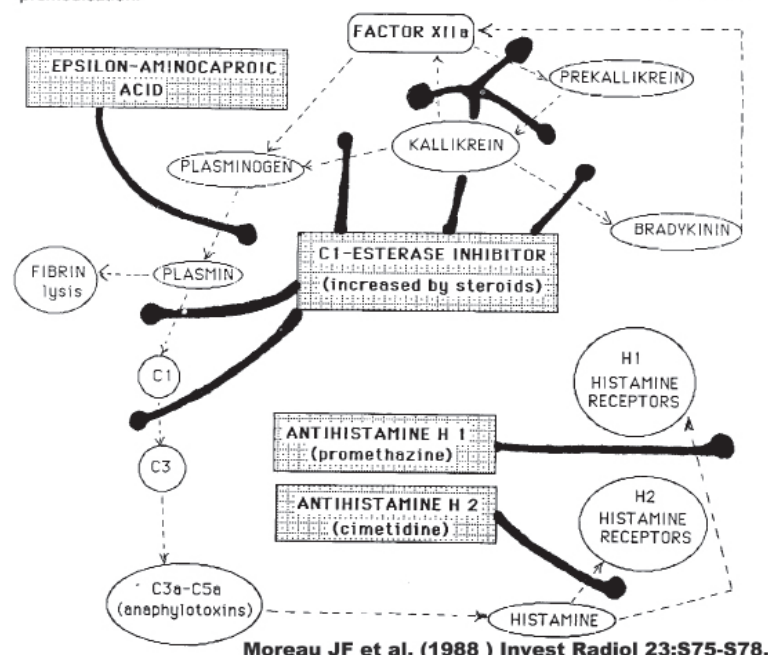


Fig. 20. Contrast media-induced reaction cascade according to Lasser modified by Moreau *et al.* showing the impact of drugs used for premedication [57].

Moreau JF *et al.* (1988) Invest Radiol 23:S75-78.

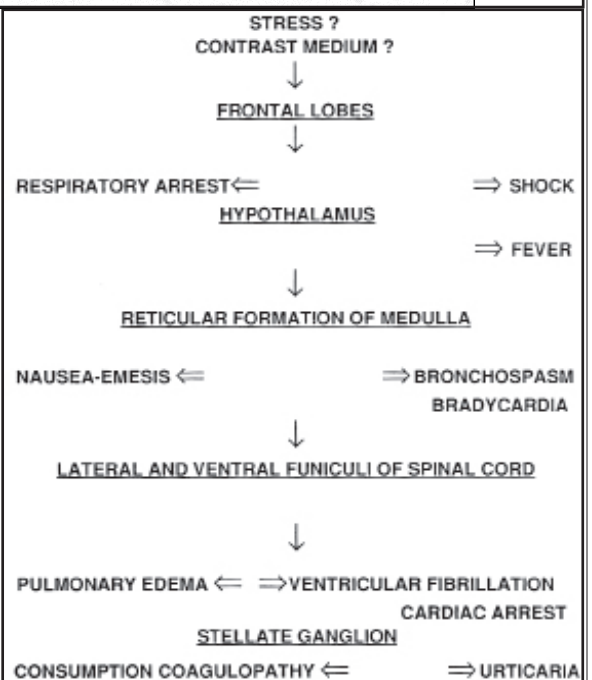


Fig. 1. Central nervous system and contrast media reactions (according to Lalli⁴).

Fig. 21. Lalli's theory of contrast media general toxicity based upon stress reaction and vaso-vagal excitation. [57]

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Clinical Survey of Adverse Reactions to Contrast Media

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CMR'87

Katayama H, Tanaka T. Clinical survey of adverse reactions to contrast media. *Invest Radiol* 1988;23(Suppl 1):S88-S89.

From October 1983 to June 1986, 33,400 individuals participated in a clinical survey of adverse reactions to conventional high osmolar contrast media. The frequency of reactions was 7.5% (2,523/33,400). No fatal cases resulted. In patients pretesting positive, the incidence of adverse reactions was 48%. In individuals with a positive history of allergy, the incidence of the reactions was 52%. There was no correlation between the incidence of reactions and the presence or absence of a history of previous contrast media administration. The value of pretesting can not be negated from the present results.

Key words: contrast media; adverse reactions; side-effect; iodinated contrast media.

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COMING SOON

Imaging in andrology

Interventional radiology

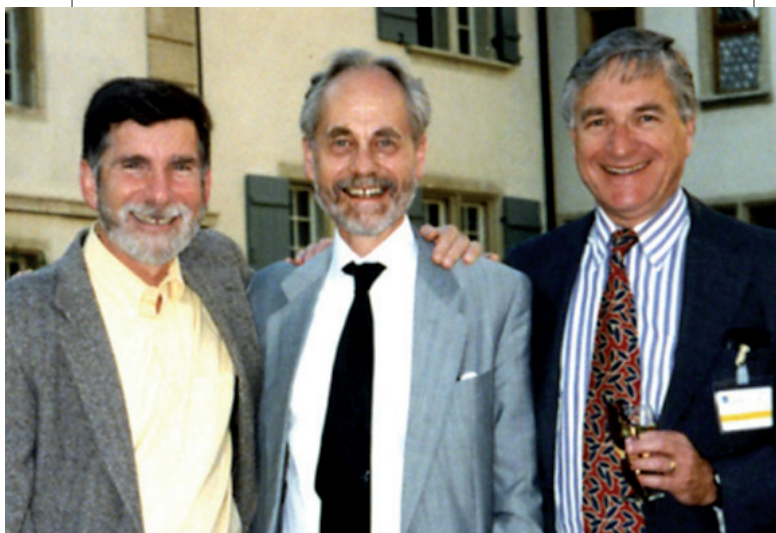
Lithotripsy

MR

Prostate imaging

Triplex doppler US

Woman's imaging...



Lee B. Talner - Thomas Sherwood - Alan J. Davidson.
(Courtesy Dr. LB Talner)