EFSUMB History of Ultrasound

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Introduction

In this review the development of ultrasound technology in Norway is summarized. Only hardware and software developments, including scanners, probes and technical solutions are covered, more on the clinical applications and their value are covered in detail in other parts of this historical review. The two Doppler prototypes, PEDOF and ALFRED developed in Trondheim were the first major contributions from Norway to the history of medical ultrasound and triggered both commercial and clinical activity on an international level. Other researchers in Norway have collaborated with industrial partners abroad. Here only technology developed mainly in Norway will be covered and work which has been published in international journals are emphasized.

Early years – Trondheim technology pioneers

An important prerequisite for the development of ultrasound imaging technology has been the link to an advanced group in acoustics or signal analysis that had been in the forefront in other fields of science and engineering. This was also the case in Norway with the largest contribution to this development rooting in the technical competence in signal analysis at the Division of Engineering Cybernetics, Norwegian Institute of Technology (NTH, now NTNU) in Trondheim.

Professor Jens Balchen leading the Division of Engineering Cybernetics, was interested in applying the institute's engineering skills to solve problems in medicine and biology. One of the engineers was Rune Aaslid, who, in collaboration with a young physician at the Regional Hospital (now St. Olavs Hospital) in Trondheim, Alf Brubakk, had undertaken work in biocybernetics making a model of the cardiovascular system based on analogue electronics (called JENNY after the first patient simulation). This collaboration lead to publications of early work on the simulation of individual patient hemodynamics (1, 2). To obtain non-invasive data on blood flow velocity and blood flow to be used in this simulation work, a young engineer, Bjørn Angelsen was employed to develop an ultrasound Doppler tool for this purpose.

Bjørn Angelsen constructed an instrument which he called PEDOF (Pulsed Echo Doppler Flowmeter) that had a series of novel features with several design solutions different from commercial Doppler units at that time. It was a combined pulsed wave Doppler (PWD) and continuous wave Doppler (CWD) with both methods incorporated in the same instrument and the same probe, most commercial units were either CWD or PWD. Its Doppler probe had two half spheres of piezoelectric crystal enabling both PWD and CWD measurement to be carried without changing or moving the probe. This probe design is still used today. It had mean and maximum velocity estimators incorporated in the unit and thus did not need a spectrum analyzer, a separate and expensive unit in the 1970's (3, 4). These estimators were based on experimental and theoretical studies of the ultrasound scattering from blood which was part of Angelsens PhD work (5-7). The maximum velocity estimator was non-directional but the mean velocity estimator included directionality and was used to impose directionality also on the maximum velocity estimator (3). Including Doppler amplitude (for timing of valve opening and closure), these two velocity curves in combination with ECG and phono signals gave a tool for noninvasive cardiac diagnoses, especially valve dysfunction. Many other Doppler design at that time utilized a narrow beam and small sample volumes for the detection of flow disturbance and turbulence around cardiac valves, Bjørn Angelsens design was different with a relative wide ultrasound beam useful for detecting the highest blood flow velocity from valve jets for calculation of the pressure gradient, pioneered by Jarle Holen, a radiologist and engineer at the National Hospital, Oslo, Norway (8, 9). He made both experimental and clinical evaluation of the use of a simplified version of Bernoullies equation in collaboration with Rune Aaslid, this proved useful for estimation of the pressure gradients across stenotic cardiac valves. He utilized a modified CW Doppler unit and a Kay Sona-Graph Sound Spectrograph and compared Doppler velocities to invasive measurements. Bjørn Angelsen, in collaboration with cardiologist in Trondheim did novel work on pressure gradient measurement with PEDOF (10, 11). Its success was based on the instrument's sensitivity rather than spatial resolution. The collaboration with Liv Hatle on this pioneering work is covered in another part of this historical review.

Building 10 prototypes of his PEDOF Doppler unit and distributing the units to major centers in Norway and abroad gave experience resulting in several new applications of Doppler measurements in clinical medicine. Angelsen employed some of his engineering student to carry out the building of these Doppler units, some of these students were later to become important contributors to the further development of ultrasound technology in Norway. The PEDOF prototype was made in two versions, 2 MHz for the heart and 6 MHz for peripheral vessels. The 6 MHz version came with probes for small vessels and a pediatric pulsed and continuous wave probe. This was the first instrument developed in Trondheim, and the 1976 PEDOF prototypes was an important milestone for the technical development of ultrasound equipment in Norway. PEDOF was constructed using analogue and dedicated logic circuitry and included analogue velocity estimators of mean and maximum velocity within the sample volume in both CWD and

PWD mode. The mean velocity estimator could be used for calculating blood flow and proved an improvement over the present zero-crossing detectors (7, 12), in addition to detect the maximum velocity within the sample volume corresponding to the spectral envelope after spectral analysis. The second Doppler unit to be designed in Trondheim was the ALFRED (All Frequency Doppler) prototypes. This unit was built by Kjell Kristoffersen and Arne Grip, two of the students involved in building the PEDOF prototypes. ALFRED incorporated many of the same features as PEDOF but had 4 different transmitting frequencies (1, 2, 5, and 10 MHz). It could therefore be used both on the heart as well as on large and small vessels. It also had a continuously variable pulse repetition frequency (PRF) with depth in the PWD mode, thus optimizing the measurable velocity at a specific depth giving a higher aliasing frequency (and therefore measurable velocity) in PWD mode. Its multiple transmitted frequencies widened the use of this Doppler unit to new fields of patient diagnosis.

Applications of PEDOF and ALFRED in addition to cardiology included obstetrics (Trondheim), cardiac surgery (Oslo and Bergen), peripheral vessels (Trondheim and Oslo) and other medical specialities, enabled Norway to be in the forefront in applying Doppler ultrasound to different patient groups.

Figure 1 **Doppler Instruments. The 1976 PEDOF (top) and 1980 ALFRED (bottom) Doppler prototypes developed in Trondheim.**

Commercialization of Trondheim prototypes

Arne Wøien, a businessman and physicist with a patent on the Hall cardiac valve prosthesis had ambitions to manufacture medical devices and equipment in Norway. Two designs of Doppler units were developed in the late 70's in Norway, PEDOF from Trondheim and UNIDOP from the National Hospital in Oslo designed by Kjell Hatteland and coworkers at the University of Oslo (13). The activity on Doppler ultrasound was coordinated through the firm Vingmed as the industrial partner set up by Wøien. The first unit from Vingmed was the commercialization of an improved version of the PEDOF which was close to the Trondheim design and manufactured in Horten, Norway from 1979. Later (1981) the ALFRED was commercialized and an improved version of both these Doppler units, called PCD 2 and PCD 4, was designed to be integrated into several cardiac scanners from different international ultrasound vendors. The unit called PCD 4 was based on the ALFRED with 4 different transmitted frequencies.

Vingmed continued to have strong links to the Trondheim group and recruiting many of its engineers and scientists from the ultrasound group in Trondheim, including the first CEO Kjell Arne Ingebrigtsen, a professor in physical electronics from NTH. Following several owners, in 1998 Vingmed was purchased by General Electric (GE) and the activity in Norway was from that date called GE Vingmed Ultrasound AS.

Further developments in collaboration with industry

DAISY (Doppler Analysis and Imaging System)

When the signal to noise ratio was poor the PEDOF analogue estimators performed less optimal than a spectrum analyzer. The Trondheim group and Vingmed therefore developed a real-time spectrum analyzer based on the new Bucket Brigade Device analogue integrated circuits which simplified the electronics of such a unit. This enabled the user to obtain the maximum velocity from the spectral curves even in patients with poor acoustic access. The DAISY was sold by Vingmed as a package with ALFRED. This type of spectral analyzer was also used in several B-mode/Doppler combinations manufactured by Vingmed.

SD100

The last stand-alone Doppler developed and manufactured by Vingmed was the SD100 which came in 1984. It was the first Doppler from Vingmed with part of the signal processing being digital and had several novel technological features. It had 4 different transmitting frequencies and a high-PRF mode which enabled higher velocities to be recorded in the PWD-mode. This is now included in most modern scanners. The new design offered a faster spectral analysis, calculation of blood flow including cardiac output, graphical analysis and trend display. Stand-alone Doppler systems without imaging has in general a better signal to noise ratio than early combined instruments and the SD100 I still used today mainly for peripheral circulation studies.

Combining Doppler with B-mode scanning

Even if the stand-alone Doppler concept was continuously improved over the years it was clear that a combination of B-mode imaging and Doppler modes would have many advantages for clinical measurements and would make the Doppler method much easier to use in clinical practice for routine patient diagnosis. We have to remember that at this point in time an ultrasound examination was routinely carried out as two separate examinations using two separate instruments, B-mode/M-mode and PWD/CWD.

In 1981 the Trondheim group made the first real-time combination where both B-mode scanning and Doppler signals were recorded simultaneously. A problem that had to be solved was what should happen with the Doppler Radio frequency signal when the scanner was active scanning a B-mode image. This was solved by constructing a Missing Signal Estimator where a Doppler signal was synthesized based on registered Doppler shifts in earlier time-windows. This was a novel invention and was first used in a combination of the PEDOF with a B-mode scanner from the American company Irex, the IrexIIIB combined instrument. This was a breakthrough in cardiac ultrasound. The principle was later published by Kjell Kristoffersen and Bjørn Angelsen (14) and the Missing Signal Estimator method was continuously improved for new combinations. An important feature of any Doppler is the quality of the filters, especially the high pass filter that remove Doppler shifted signals from slowly moving tissue. Improved filters were developed by Kjell Kristoffersen and later new filters for color flow applications by Hans Torp (15, 16). Hans Torp contributed especially to the signal analysis for color Doppler which was included in the next generation of B-mode/Doppler combination. Hans Torp should later become the group leader of the ultrasound activity in Trondheim.

Combining Color Doppler with B-mode scanning

The Trondheim group and Vingmed had ambitions to develop a scanner in Norway and the first scanner from Vingmed was the CFM700 (CFM – Color Flow Mapping) series with tilting annular array probes. Annular array mechanical probes have its advantages and disadvantages, dynamic focusing in two planes (in the lateral and azimuthal directions) was an advantage, but because of the mechanical movement of the active parts of the probe, frame rate was in general lower than for a phased array probe. This was not so important for imaging stationary and slowly moving organs. As the name indicate the CFM series had real-time color flow Doppler mode, a method pioneered in Japan and introduced into the market by Aloka in 1983. The CFM700 was the first ultrasound scanner built in Norway and was launched at the American College of Cardiology meeting in Atlanta, USA, in March 1986.

The next scanner from Vingmed was the System 5, their first scanner with electronic transducers and introduced in 1995. It included linear, curvilinear, phased array probes and annular arrays probes in addition to input for intracardiac/intravascular ultrasound catheters (17). It was thus a versatile instrument for use in many medical disciplines. The spectrum analyzer based on the original DAISY concept was now replaced by a digital signal processor in line with the increased digitalization of the signal processing in ultrasound instruments. The System 5 was given the EU commission “Information Technology Award” for the most innovative IT product in 1995. A comprehensive textbook summing up the signal analysis of both Doppler and combined instruments was published by Bjørn Angelsen in 1996 (18)

Figure 2 **Vingmed CFM700. The first ultrasound scanner developed and manufactured in Norway, the Vingmed CFM700 annular array scanner.**

Figure 3 **System 5. The first ultrasound scanner from Vingmed with electronic probes.**

Applications of ultrasound technology developed in Norway

In this chapter, the technology developed for the different applications will be considered, for the more clinical use and benefits, see other chapters of this historical review. Two important clinical collaborators between the engineering group and clinicians in Trondheim were cardiology and obstetrics at the Regional Hospital in Trondheim, who by this close cooperation also contributed to the design of different probes and functional improvements of several instruments. This also spread to other medical disciplines.

Cardiology

The close cooperation between Bjørn Angelsen and Liv Hatle lead to several novel applications in cardiology and to the further development of the Doppler methods to diagnose valve disease. Other new probes and signal processing includes 3D tilting and rotational mechanical scanning (19) and the development of on-line Tissue Velocity Imaging (TVI). The TVI method was first published by Isaaz in 1989 (20) followed by McDicken and Sutherland in 1992 (21). The first measurement of strain and strain rate was published by Heimdal and coworkers from the Trondheim group in 1998 (22), later evaluated in ischemic patients by Asbjørn Støylen (23).

Obstetrics

Sturla Eik-Nes came to Trondheim in 1979 and pioneered many applications and research in obstetrical ultrasound in collaboration with Bjørn Angelsen's group. He later established the Norwegian Center for Fetal Medicine. This important collaboration lead to publications on blood flow measurements using a combination Doppler/B-mode in 1981 (24). During the 80's special probes developed for obstetrics was developed and the annular array probes used for the CFM700 and System 5 scanners was particularly useful in obstetrics both for transcutaneous and transvaginal applications because of the improved 2-plane beam focusing. A mechanical 3D transvaginal probe was developed with superior image resolution and enabled studies of embryos less than 10 mm to be studied, published by Harm-Gerd Blaas in 1998 (25), after an evaluation of the probe resolution and results in phantoms was carried out (26). Also flow studies of the fetal ductus venosus was published using the CFM700 scanner by Torvid Kiserud (27).

Peripheral circulation and coronary vessels

The possibility to use high frequency transmission with some of the Trondheim prototypes gave a tool to study peripheral vessels. Einar Stranden and coworkers at the Aker Hospital in Oslo used Doppler ultrasound in combination with other methods to evaluate peripheral circulation (28). He was also involved in the design of the System 5 scanner while employed at Vingmed. At the National Hospital in Oslo, Department of Neurosurgery, Arne Grip designed special purpose equipment for blood flow studies related to neurosurgery (29). At Haukeland Hospital in Bergen several special purpose Doppler probes was designed and Knut Matre and Leidult Segadal published work using these probes in cardiac surgery both for detecting coronary arteries and for measuring blood flow in coronary bypass grafts, some of these probes were manufactured by Vingmed (30). Also probes for intraluminal flow velocity profile studies were designed, these were also used as a reference for the evaluation of CFM velocity profile methods (31, 32).

Gastroenterology

At Haukeland Hospital/University of Bergen, Gastroenterology, the ultrasound group headed by Svein Ødegaard designed new methods for ultrasound evaluation of the GI-tract. Doppler probes to be introduced via the biopsy channel of an endoscope was used for studying vessels in the gastric wall (33). The 3D mechanical system for the System 5 scanner designed originally for the heart, and a 3D system based on a position sensor set-up from Flock of Birds, USA, both systems developed in Trondheim, were used for 3D visualization of the stomach (34, 35). Also, a modified System 5 with filter settings suitable to track the slow contractions of the GI tract was used by Odd Helge Gilja for TVI strain measurements of the contracting gastric wall to diagnose functional gastric disorders (36).

Other spin-offs from the Trondheim group

Much of the further development of ultrasound technology in Norway outside cardiology were related to the Trondheim pioneering group including further work carried out by persons involved in the initial research group.

Intracranial Doppler

Rune Aaslid carried out the first intracranial Doppler velocity recording and went on to develop special purpose Doppler and scanners for intracranial applications. By reducing the transmitted frequency,increasing the intensity and improved focusing he was able to obtain Doppler signal from the basal cerebral arteries from a trans-temporal approach, first published in 1982 (37). This was further developed into a special purpose Doppler for intracranial measurements manufactured by Eden Medizinische Elektronik, Germany, with Aaslid working from Bern, Switzerland.

Transit-time flowmeter

Arne Grip, after working at the Departments of Neurosurgery and Cardiac Surgery, National HospitaL OF Oslo, Norway, developed an ultrasound transit-time flowmeter for accurate flow measurements in exposed vessels during vascular and coronary bypass surgery. This was commercialized through Medistim A/S and became one of the most popular flow measurement tools in this field. Arne Grip developed this tool further with combining the transit-time flowmeter with PWD and finally with a linear array probe for B-mode and color Doppler.

Education, events and congresses

First course in medical ultrasound held in Trondheim in January 1979

This was an important meeting for the collaboration across medical disciplines and between the engineering and medical field in a small country like Norway. Hosted by several societies in medicine and engineering, many fields of medicine were represented. Radiologists, cardiologists, obstetricians, cardiac and vascular surgeons, neurologist, in addition to a large number of engineers and physicists made it clear that many of the technical issues with introducing new ultrasound methods in clinical practice, including the new Doppler methods, was common across the different medical disciplines. This meeting was an important event for research in ultrasound diagnosis and especially important for the introduction of Doppler methods outside cardiology in Norway.

Conclusion, summary

One of the most important factors for the success of the development of ultrasound technology in Norway was the close collaboration between clinicians and engineers in Trondheim. This led to continuous modifications of existing instruments as well as new developments based on clinical experience. Also, the good collaboration across medical disciplines in a small country like

Norway made it easier to adopt and apply these methods also outside cardiology and obstetrics. Having the first Doppler unit and scanner commercialized by a Norwegian company was also a major contributor to the further development of ultrasound technology in Norway.

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