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Breath emulator for simulation and modelling of expired tidal breath carbon dioxide characteristics

Lewis Fleming¹, Des Gibson¹*, David Hutson¹, Sam Ahmadzadeh¹, Ewan Waddell¹, Shigeng Song¹, Stuart Reid², Caspar Clark³, Julian S Baker⁴, Russell Overend⁵, Calum MacGregor⁶

¹Institute of Thin Films, Sensors and Imaging, School of Engineering and Computing, University of the West of Scotland, PA1 2BE Paisley, Scotland, UK

²The department of Biomedical Engineering, Graham Hills Building, The University of Strathclyde, 50 George Street, Glasgow, G1 1QE, UK

³Helia Photonics Ltd, Unit 2, Rosebank Technology Park, Livingston, EH54 7EJ, UK

⁴Hong Kong Baptist University, Kowloon Tong, Hong Kong, P R China

⁵Wideblue Ltd, Kelvin Campus, West of Scotland Science Park, Glasgow, G20 0SP

⁶Gas Sensing Solutions Ltd, Westfield North Courtyard, Glasgow G68 9HQ, UK

AUTHOR INFORMATION

Lewis.Fleming@uws.ac.uk
Des.Gibson@uws.ac.uk
David.Hutson@uws.ac.uk
ewan.waddell@btinternet.com
Shigeng.Song@uws.ac.uk
Sam.Ahmadzadeh@uws.ac.uk
Stuart.Reid@strath.ac.uk
Caspar.Clark@helia-photonics.com
JSBaker@hkbu.edu.hk
russell.overend@wide-blue.com
calum.macgregor@gassensing.co.uk

*Corresponding Author
Des.Gibson@uws.ac.uk
Telephone number: +44 (0)141 848 3610
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³Helia Photonics Ltd, Unit 2, Rosebank Technology Park, Livingston, EH54 7EJ, UK

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⁶Gas Sensing Solutions Ltd, Westfield North Courtyard, Glasgow G68 9HQ, UK

AUTHOR INFORMATION

Lewis.Fleming@uws.ac.uk

Des.Gibson@uws.ac.uk

David.Hutson@uws.ac.uk

ewan.waddell@btinternet.com

Shigeng.Song@uws.ac.uk

Sam.Ahmadzadeh@uws.ac.uk

Stuart.Reid@strath.ac.uk
Caspar.Clark@helia-photonics.com

JSBaker@hkbu.edu.hk

russell.overend@wide-blue.com

calum.macgregor@gassensing.co.uk

*Corresponding Author

Des.Gibson@uws.ac.uk

Telephone number: +44 (0)141 848 3610
ABSTRACT

BACKGROUND: In this work we describe a breath emulator system, used to simulate temporal characteristics of exhaled carbon dioxide (CO₂) concentration waveform versus time simulating how much CO₂ is present at each phase of the human lung respiratory process. The system provides a method for testing capnometers incorporating fast response non-dispersive infrared (NDIR) CO₂ gas sensing devices - in a clinical setting, capnography devices assess ventilation which is the CO₂ movement in and out of the lungs. A mathematical model describing the waveform of the expired CO₂ characteristic and influence of CO₂ gas sensor noise factors and speed of response is presented and compared with measured and emulated data.

OBJECTIVE: A range of emulated capnogram temporal waveforms indicative of normal and restricted respiratory function demonstrated. The system can provide controlled introduction of water vapour and/or other gases, simulating the influence of water vapour in exhaled breath and presence of other gases in a clinical setting such as anaesthetic agents (eg N₂O). This enables influence of water vapour and/or other gases to be assessed and modelled in the performance of CO₂ gas sensors incorporated into capnography systems. As such the breath emulator provides a means of controlled testing of capnometer CO₂ gas sensors in a non-clinical setting, allowing device optimisation before use in a medical environment.

METHODS: The breath emulator uses a unique combination of mass flow controllers, needle valves and a fast acting switchable pneumatic solenoid valve (FASV), used to controllably emulate exhaled CO₂ temporal waveforms for normal and restricted respiratory function. Output data from the described emulator is compared with a mathematical model using a range of input parameters such as time constants.
associated with inhalation/ exhalation for different parts of the respiratory cycle and CO2 concentration levels. Sensor noise performance is modelled, taking into account input parameters such as sampling period, sensor temperature, sensing light throughput and pathlength.

**RESULTS:** The system described here produces realistic human capnographic waveforms and has the capability to emulate various waveforms associated with chronic respiratory diseases and early stage detection of exacerbations. The system has the capability of diagnosing medical conditions through analysis of CO2 waveforms. Demonstrated in this work the emulator has been used to test NDIR gas sensor technology deployed in capnometer devices prior to formal clinical trialling.

**Keywords:** capnography, capnometer, NDIR, carbon dioxide sensor, III-V, mid-infrared

**INTRODUCTION**

Capnometry has been a standard medical technique for the past thirty years, providing assessment of the human lung respiratory process through measurement of carbon dioxide (CO2) in exhaled air movement in and out of the lungs [1]. The technique is traditionally limited to acute clinical care and anaesthesiology, primarily due to the high cost of capnometers and the integrated systems into which data is displayed. Moreover, the previous capnometers are limited in that their response times are relatively slow, exhibit poor accuracy at low concentrations of CO2 and do not cope well with water vapour in exhaled breath.
Respiratory disease is one of the top five chronic diseases internationally, according to the World Economic Forum. The principal respiratory diseases consist of chronic obstructive pulmonary disease (COPD), asthma, congestive heart failure, lung cancer, pulmonary embolisms, emphysema and cystic fibrosis. Many of these respiratory diseases are chronic and debilitating, with side effects such as depression and anxiety. Many respiratory conditions, especially asthma, are poorly managed particularly with respect to adherence to medicines regimes.

The diagnosis of respiratory conditions is notoriously difficult. Primary care physicians have difficulty in distinguishing between the various respiratory diseases due to the inter-relationship and degree of interpretation required by the various tests, which include peak-flow, spirometry, arterial blood gas analysis, x-rays and pulse oximetry.

This fact was recognised in the United Kingdom National Health Service Five Year Forward View Strategy of 2014 [6]. Improving the diagnosis and treatment of respiratory disease was identified as one of the primary targets to reduce costs and mortality.

There have been a significant number of papers in peer-reviewed medical journals regarding the need to widen the usage of capnography to include Expired Tidal Breathing CO2 (ETBCO2) waveform biomarker analysis to diagnose the disease state of respiratory conditions [7], [8]. Papers have been published about the characteristics of this under used biomarker in providing diagnosis and management of cardiorespiratory disorders such as COPD, asthma, congestive heart failure, pulmonary embolism and emphysema. These studies indicate the ETBCO2 waveform biomarker is unique to the
individual and is modified by the respiratory disease and the current disease state [9]–[12].

Need for such fast and low cost CO$_2$ sensors used within capnometers as portable point of care respiratory disease diagnosis systems, based on ETBCO2 waveform biomarker, has been recently reviewed with a specific focus on an asthma monitoring device [13]. Commercially available time-based capnographs are bulky, costly and not suited to point of care use. During the last decade only a few studies have been conducted to overcome the limitations of existing capnography and developing capnography in line with cardiorespiratory analysis.

When developing a capnograph, choosing an appropriate CO$_2$ sensor plays a vital role and remains challenging in line with the application, cost, accuracy, speed of response and sensitivity with several CO$_2$ sensor technologies are available to measure CO$_2$ during respiration. [14]–[16]. Among them, a low-cost yet sensitive technique is Non-Dispersive Infrared (NDIR) spectroscopy [17]. Reference [13] provides an overview of a wide range of low-cost NDIR CO$_2$ sensor modules with their corresponding specifications.

This works describes a breath emulator system for simulation and modelling the ETBCO2 and respiration rate of exhaled carbon dioxide, removing the need for direct human patient measurements during CO$_2$ sensor development and optimisation. The breath emulation system described in this work is shown to reproduce complex ETBCO2 waveform patterns that match those measured in the clinical environment and use for characterising CO$_2$ sensors used within capnometers. Clinical studies comparing two capnometers marketed for emergency medicine found that only one met the
requirements for informative and regular use, highlighting a need for improved and standardised capnometer testing capabilities [20].

The system described in this work allows a large degree of user control over the output CO₂ waveform by utilizing a combination of mass flow controllers, needle valves and a fast acting switching valve. The system also includes a heater and bubbler combination to respectively mimic the temperature and humidity inherent in human exhalations. A facility for introduction of anaesthetic gas is also included for testing capnometer sensor response to nitrous oxide, a popular anaesthetic gas used for general anaesthesia. Discussed in more detail below, no such combination of features has before been integrated into a single breath emulation system. The breath emulator in this work is demonstrated using a fast response NDIR sensor [22] and currently in clinical trials for point of care capnography [23].

METHODS & MATERIALS

Setup

The gas flow circuit for the system, referred to as the Capnometry Test Rig is shown in figure 1.
Figure 1. Gas flow circuit diagram for the capnometry test rig indicating, dry air, CO₂, wet air, mixed gases and anaesthetic gas feed lines.

The red line depicts air inlet 1. Air can be fed in from a gas cylinder, such as a 78% nitrogen/21% oxygen mixture and must be free of contamination as any contaminant making its way into the CO₂ gas sensor will disrupt the signal, explained in further detail below. The flow bifurcates into two lines, one line is directed through a manifold purge valve (D) and upon exiting is mixed with CO₂ from inlet 2. The other line passes through an Omega FMA4500 Series 1000 L·min⁻¹ mass flow controller. The user has the option of passing the air through the bubblter – a tank of water in which H₂O vapour is picked
up by the air flow to mimic the near 100% relative humidity of exhaled breath. The bubbler can be bypassed by closing the humidifier bypass and humidifier isolate valves, (B) and (C) respectively. The air or air/H₂O gas mixture is then fed through an Omegalux 1000 W AHPF-102 Series circulation heater for low flow air with a heated length of 203 mm and total length of 254 mm. The temperature can be varied; however during operation 37°C is often used to mimic the temperature of the human breath. Next the flow is directed through multiple coils of tubing and through the rotameter (Line 1) to the 3 port FASV. Temperature and Humidity are measured with a temperature and humidity sensor (T, RH) and are reported to a read-out on the graphical user interface. The coils of tubing are introduced to increase the volume of the gas manifold to represent the volume of the gas containing spaces of the human lung, which ultimately have an impact on the shape of the capnogram waveform. Later, line 2 was severed and a 100 ml plastic syringe was introduced to give the user a variable control of the volume of the manifold.

The dark green line (inlet 2) depicts the CO₂ gas feed. CO₂ can be fed from a gas cylinder and is directed through a second Omega FMA4500 Series 200 L·min⁻¹ mass flow controller and is mixed with air from inlet 1. The air/CO₂ mixture flow then moves through the rotameter labelled line 2 and into the 3 port FASV. Inlet 3 is for the anaesthetic gas feed, such as N₂O, and is controlled via use of a needle valve – if enabled, the anaesthetic mixes with the air/CO₂ mixture in the mixed gases line and is directed through line 2.
Lines 1 and 2 feed into a pneumatic solenoid valve which is controlled via software written to control the whole system. The pneumatic solenoid valve acts as a fast acting switching valve which switches the output between lines 1 and 2, delivering a mixture of air and mixed gases to the part under test. When the output comes from line 2, the CO$_2$ concentration at the part under test, which is typically a CO$_2$ gas sensor, rises to a maximum concentration ultimately determined by the CO$_2$ partial pressure in line 2. When the valve is switched, and the output comes from line 1, pure air (or an air/water vapour mixture) is delivered to the gas sensor, having the effect of reducing any CO$_2$ concentration by displacing the volume already present inside the sensor.

This periodic rising and falling of CO$_2$ concentration recorded by the gas sensor represents the movement of air between the environment and the lungs via inhalation and exhalation and is synonymous with emulated breathing. The shape of the emulated waveform can be controlled by changing the switching frequency of the FASV and by tweaking the CO$_2$ needle valve and rotameter valves on lines 1 and 2.
Figure 2. Inside of capnometry test rig showing MFCs, bubbler for relative humidity, heater, gas inlets, PAC, control circuitry and syringe and tubing coils.

From figure 2 the air, CO₂ and anaesthetic feeds can be seen at the top right of the apparatus. The separate air and CO₂ lines feed into the air and CO₂ mass flow controllers respectively. From the air MFC, the line feeds into the bubbler with the option of a bypass then through the heater and into the tubing coils. The CO₂ line goes directly into the tubing coils where it is mixed with the air. Two separate feeds come from the tubing coils and into lines 1 and 2, one containing mixed air and CO₂ and the other only air. The mixed air and CO₂ line passes a plastic syringe, with the purpose if increasing the volume of the manifold before reaching the FASV and output.
The rotameters on lines 1 and 2 can be seen in figure 3, as well as the control screen and system control valves including; the humidifier enable, isolate and bypass valves, the manifold purge and manifold vent valves, the CO₂ isolate and needle valves, the anaesthetic valve and the air isolate valve. The top right of the system contains the control circuitry and a Celduc SG444020 phase angle controller (PAC) used to provide a variable power output for controlling the MFC’s, heater and FASV for control. Data is fed back to the readout via an Arduino microcontroller. On the left-hand side of system, the output feeds into a GSS SprintIR CO₂ gas sensor which records CO₂ concentration data and sends to the readout on the user interface. The user can remove the sensor and include a different test part such as a capnometer.

**Figure 3.** Front face of Capnometry Test Rig, showing vent, isolation, purge and needle valves along with rotameters and user interface.
The SprintIR is a high speed CO\textsubscript{2} gas sensor with an operating range of 0 \% to 100 \%, taking 62 measurements per second [22]. The sensor has a standard digital output which is displayed on the Plot CO\textsubscript{2} screen on the user interface. Figure 5 shows a schematic of the sensor. The SprintIR is a non-dispersive infrared (NDIR) sensor, with a light emitting diode and a photodiode situated at opposite ends of a rectangular bridgeboard [17]. The LED emits a band of IR radiation centred at a wavelength of 4300 nm into the dome, which reflects of a gold coated optic. The reflected light is then incident on a photodiode which produces a photocurrent proportional to the intensity of the incident light. The CO\textsubscript{2} molecule has an absorption band centred around 4300 nm, therefore any CO\textsubscript{2} inside the sensor will absorb the IR light resulting in a proportionally diminishing photodiode photocurrent with increasing CO\textsubscript{2} concentration [17]. The sensor can be inserted directly onto the output, thereby giving a good indication of what
a mainstream capnometer would see. Recent reviews [24] suggest that mainstream capnography is advantageous over side-stream due to current generation devices being relatively light, low in dead space, having better signal fidelity and better ETCO₂ measurements at faster respiratory rates such as those observed in small children [25].

RESULTS

The normal capnogram has multiple features that allow for clinical interpretation, however there are currently no standards for labelling the normal capnogram.

The normal time capnogram is reproduced by the Capnometry Test Rig as shown in figure 3. It can be seen that the system is capable of producing the four standard phases of the classic capnogram including realistic numerical values such as the 0% CO₂ concentration measured at the respiratory baseline and approximately 4% concentration of ETCO₂.
Figure 8. Normal capnogram generated using the breath emulation system, showing the standard capnogram phases 0, I, II and III.

Figure 9 depicts a series of capnograms indicative of various pathologies, medical interventions and phenomenon often encountered during the measurement of ETCO$_2$. These capnograms were produced using the breath emulation system described in the above section. Pathologies are listed in table 1.
Figure 10. Measured time capnogram.

Table 1

<table>
<thead>
<tr>
<th>Capnogram</th>
<th>Phenomenon</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Normal CO2 waveform [27]</td>
</tr>
<tr>
<td>B</td>
<td>Hyperventilation [28]</td>
</tr>
<tr>
<td>C</td>
<td>Hypoventilation [29]</td>
</tr>
<tr>
<td>D</td>
<td>Rebreathing</td>
</tr>
<tr>
<td>E</td>
<td>Emphysema [30, 31, 32]</td>
</tr>
<tr>
<td>F</td>
<td>Paediatric capnogram [30]</td>
</tr>
<tr>
<td>G</td>
<td>Slit in sampling tube [33]</td>
</tr>
<tr>
<td>H</td>
<td>Esophageal intubation [34, 45]</td>
</tr>
</tbody>
</table>
Infrared CO$_2$ monitoring has been introduced for clinical use due to easy handling and sufficient accuracy [36], [37] and is consistent with other gas measurement modalities such as mass spectrometry. Infrared CO$_2$ gas monitors exhibit a degree of signal cross-talk with other gaseous species that have their absorption bands neighbouring the CO$_2$ absorption band centred at a wavelength of 4260 nm. This is also the case with the GSS SprintIR CO$_2$ gas sensor discussed in the previous section. The sensor’s total signal is given by the area underneath the curve of the convolution of the LED emission and photodiode detection spectral responses. This is shown by the red curve in figure 9. When CO$_2$ is present, absorption of the IR signal takes place, reducing the total area below the spectral response curve and reducing the overall signal. The blue and green curves show CO$_2$ and N$_2$O absorption coefficients occurring at central wavelengths of 4260 nm and 4500 nm respectively. As a result of the overlap between the LED/PD spectral response and the N$_2$O absorption band, the sensor is also sensitive to N$_2$O, however, not as strongly as CO$_2$, as the N$_2$O band absorbs lesser signal due to being upshifted from the LED/PD spectral response central peak and also due to N$_2$O having lower total cross-section [38].
Nitrous oxide (N\textsubscript{2}O) is a widely used gas used for analgesia and surgical anaesthesia and is typically delivered to patients in concentrations of up to 70% in a mixture with oxygen and often more potent anaesthetics to produce general anaesthesia [sher1984, emmanoiul2007]. The introduction of N\textsubscript{2}O into the manifold allows the user to test a device’s response when N\textsubscript{2}O is included in the air/CO\textsubscript{2} mixture. Figure 13 shows the CO\textsubscript{2} sensor value when both CO\textsubscript{2} and N\textsubscript{2}O are fed into the system. The black CO\textsubscript{2} sensor value curve depicts a normal time capnogram and was obtained by feeding a standard air/CO\textsubscript{2} mixture into the manifold with the anaesthetic valve closed. Next, N\textsubscript{2}O was fed in and
the anaesthetic valve opened. The result is shown by the green CO₂ sensor value with anaesthetic N₂O feed curve. It can be seen that the N₂O introduces a significant and erroneous reported increase in ETCO₂ value as detected by the gas sensor.

Figure 13. Effect of N₂O introduction on measured capnogram shape, when N₂O is added to the air/CO₂ gas mixture using the NDIR sensing technique.
As mentioned above, water vapour in high concentrations can result in erroneous CO₂ readings from the gas sensor. It is known that exhaled breath has a relative humidity of 100% due to water diffusing across the moist surface of breathing passages and alveoli [dery1971]. The mass of water vapour a pocket of air can contain is dependent upon its temperature; the mean breath temperature of end-expired breath is approximately 35°C [cowan2010], therefore delivering warm, wet air to the sensor can result in a high concentration of water vapour present inside the sensor's optical cavity. The dominant impact water vapour has on the sensor response is due to scattering of IR radiation as a result of water vapour that has condensed on the Au coated optical surface.

Capnogram J in figure 14 is a normal emulated capnogram obtained in the same way as capnogram A in figure 3. To demonstrate the effect of a warm and wet air/CO₂ mixture on the recorded capnogram shape, the heater and bubbler were enabled, with boiled water being added to the bubbler.

Initially, the effect of enabling the bubbler is shown in capnogram K. At a temperature of 20°C and a relative humidity of 99% it can be seen that the ET CO₂ gradually increases. As the temperature rises, the density of water vapour also rises and at a temperature of 25°C and a relative humidity of 100% it can be seen that the reported ET CO₂ level continues to rise and maxes out at the sensor limit of 10% in capnogram L. It is also seen that the measured respiratory baseline begins to elevate above 0% even when the sensor should be filled with air.

It is suspected that the photocurrent produced by the photodiode increases as IR radiation is scattered away by condensed water vapour and no longer incident on the photodiode surface regardless of the lack of presence of CO₂. When CO₂ is present, we
believe that the combined effect of \( \text{CO}_2 \) induced IR absorption and condensed water vapour scatter causes the dramatic increase in both maximal ETCO\(_2\) and the respiratory baseline.

**Figure 14.** Emulated CO\(_2\) versus time plots for 20\(^\circ\)C, 99\% RH and 25\(^\circ\)C, 99\% RH.

**MODELLING AND SIMULATION**

Demonstrated in this work, the system has been used to test an NDIR CO\(_2\) gas sensor [17,22] used in a point of care capnometer currently undergoing formal clinical trials.

The CO\(_2\) concentration waveform versus time - how much CO\(_2\) is present at each phase of the human lung respiratory process – can be considered as three distinct stages.

1. Exhalation (exponential rise)
2. Expiratory plateau (linear increase)
3. Inhalation (exponential fall)
Stages 1 and 3 have different rise and fall time constants. Specific curve fitting parameters are provided in the following table with symbols as used in the curve fitting equation –

<table>
<thead>
<tr>
<th>Parameter (unit)</th>
<th>Symbol</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Window Interval (s)</td>
<td>Ts</td>
<td>30</td>
</tr>
<tr>
<td>Breath Rate (Breaths per minute)</td>
<td>R_b</td>
<td>17</td>
</tr>
<tr>
<td>Exhalation Time (s)</td>
<td>t_ex</td>
<td>2.2</td>
</tr>
<tr>
<td>Inhalation Time (s)</td>
<td>t_in</td>
<td>2.8</td>
</tr>
<tr>
<td>Minimum CO₂ Concentration (ppm)</td>
<td>CO₂_{min}</td>
<td>5000</td>
</tr>
<tr>
<td>Maximum CO₂ Concentration (ppm)</td>
<td>CO₂_{max}</td>
<td>52348</td>
</tr>
<tr>
<td>Time Constant Exhalation (s)</td>
<td>τ_{ecX}</td>
<td>0.28</td>
</tr>
<tr>
<td>Time Constant Inhalation (s)</td>
<td>τ_{inc}</td>
<td>0.21</td>
</tr>
<tr>
<td>Sampling Period (s)</td>
<td>t_{sam}</td>
<td>0.01</td>
</tr>
<tr>
<td>Time constant inhalation slope in high CO₂ region</td>
<td>α</td>
<td>0.045</td>
</tr>
</tbody>
</table>

Table 1 – Model fit parameters and typical values for normal breath

Specific curve fit incorporating the three stages is shown in the following equation -

\[
CO₂_{\text{peak}} = (CO₂_{\text{max}} - CO₂_{\text{min}}) \times \left[ 1 - e^{\left(-\text{mod}(\tau_{ex} - \tau_{s}), \tau_{s}\right)} \right] \times \left( 1 + \alpha \times \text{mod}(\tau_{ex}, \tau_{s}) \right) + CO₂_{\text{min}}
\]

Noise factors are calculated from a comprehensive sensor model and multivariate regression used to derive noise as function of concentration and integration time [17].

Actual breath was measured using a fast response NDIR sensor [22] with characterised Johnston, dark current, quantisation and shot noise noise parameters [17, 39]. Comparison of measured, modelled (fit parameter values shown in above table 1) and emulated waveforms are shown in the following Figures 15 and 16 for single and multiple breaths respectively.
CONCLUSION

It has been shown the breath emulator system described above has the capability of producing configurable capnogram temporal waveforms indicative of normal and restricted respiratory function encountered in clinical capnography. The breath
emulator system also has the capability to emulate the effect of cross-talk induced by anaesthetic gas, temperature and humidity. Operation for normal breath is demonstrated with good agreement between measured, modelled and emulated.

Future work it is suggested that the CO\textsubscript{2} and N\textsubscript{2}O needle valves be replaced with valves that have a numerical readout, thereby providing enhanced control over the output waveform. As it stands, no such readout is available for these valves and the user must obtain desired values of ETCO\textsubscript{2} and capnogram shape by trial and error. The current system uses the same curve fitting parameters averaged over multiple breaths with a future system improvement providing on the fly curve fitting to enable tracking of breath by breath changes.

A future breath emulator modification is underway to allow oxygen, CO\textsubscript{2} and breath flow to be incorporated.

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**REFERENCES**


01/06/2020

Dear Prof. Filippo Molinari,

We have no conflicts of interest to disclose.

Sincerely,

Professor Des Gibson
Director – Institute of Thin Films, Sensors & Imaging