Gold Nanoparticle Sensors For Detecting Chronic Kidney Disease and Disease Progression

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ABSTRACT

Aim: To study the feasibility of a novel nanomedical method that utilizes breath testing for identifying chronic kidney disease (CKD) and disease progression. **Materials & Methods:** Exhaled breath samples were collected from 62 volunteers. The breath samples were analyzed using sensors based on organically functionalized gold nanoparticles, combined with support vector machine analysis. Sensitivity and specificity with reference to CKD patient classification according to estimated glomerular filtration rate were determined using cross-validation. The chemical composition of the breath samples was studied using gas chromatography linked with mass spectrometry. **Results:** A combination of two to three gold nanoparticles sensors provided good distinction between early-stage CKD and healthy states (accuracy of 79%) and between stage 4 and 5 CKD states (accuracy of 85%). A single sensor provided a distinction between early and advanced CKD (accuracy of 76%). **Conclusion:** Breath testing using gold nanoparticle sensors holds future potential as a cost-effective, fast and reliable diagnostic test for early detection of CKD and monitoring of disease progression.

INTRODUCTION:

A novel method for identifying chronic kidney disease (CKD) and disease progression was explored that utilizes breath testing. CKD depicts progressive loss of kidney function over a period of months or years. The accurate determination of the kidney function is essential for the treatment of CKD, for identifying patients with early renal impairment and for following the course of established disease. Recent guidelines classify the severity of CKD in five stages according to the reduction in glomerular filtration rate (GFR), with stage 1 being a mild illness and stage 5 being a severe illness. Retained Urea and Creatinine serve as markers of kidney failure. Moreover, up to 60% of the kidney function may be lost before serum creatinine begins to rise.

Aim: To study the feasibility of a novel nanomedical method that utilizes breath testing for identifying CKD and disease progression. **Methods:** A cross-sectional comparative survey. 62 volunteers, aged 22–83 years, who had sufficient clinical and biochemical data for inclusion, were recruited. These were 17 patients with intermediate CKD (stage 2 and 3), 20 patients with advanced CKD (stage 4 and 5) and 15 healthy controls. Breath samples were collected and were analyzed using acustom-designed, nanoscale artificial, combined with support vector machine (SVM) analysis,to detect statistically significant differences between the sub-populations. Sensitivity and specificity were determined using cross-validation. The chemical composition of the breath samples was studied using gas chromatography linked with mass spectrometry (GC-MS).

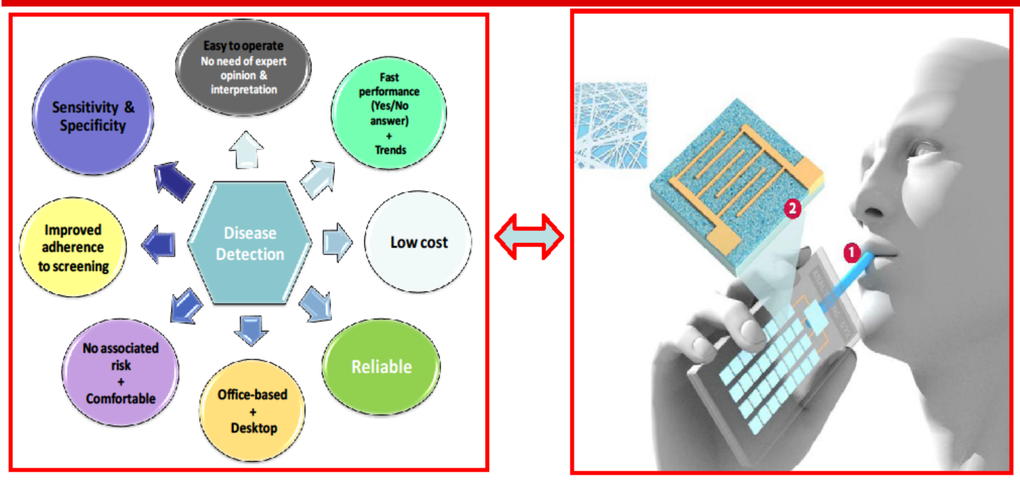
RESULTS:

The feasibility of the GNP sensors for diagnosing the early-stages of CKD was tested by comparing breath samples of 17 patients with stage 2 and 3 CKD to breath samples of 15 healthy controls. In this way, one sensing feature of sensor S1 (F1) and three independent features of sensor S2 (F1, F2 and F4) were selected through SVM for the distinction between stage 2 and 3 CKD patients and healthy controls. The sensors S1 and S2 were selected because they were the most capable sensors among the reservoir of 20 GNP sensors for discriminating between the two groups. SVM analysis determined a suitable set of five sensing features from sensors S1, S3 and S4 for the distinction of stage 4 and 5 CKD patients. These were three independent features of sensor S1 (F2–F4), one feature of S3 (F2) and one feature of S4 (F1). Very good separation between stage 4 and 5 CKD states was achieved with these sensing features. The progression from early-stage (stage 2 and 3) to late-stage (stage 4 and 5) CKD was determined using a single sensing feature of sensor S1. The chemical composition of the exhaled breath of CKD patients was analyzed and compared with the breath of healthy controls, using GC-MS.

CONCLUSIONS:

1. We have delivered a proof-of-concept for a novel method in nanomedicine for detecting early-stage CKD and monitoring disease progression from exhaled breath of patients.
2. Suitable combinations of GNP sensors could identify with high accuracy patients with early-stage CKD and determine disease progression from advanced CKD to ESRD..
3. Transition from early disease (stages 2 and 3) to advanced disease (stages 4 and 5) could be identified from a single sensing feature.

Fig.1: A Nanomedical Device for Screening and Diagnosing Diseases



The main features that will be fulfilled by the **NA-NOSE** for screening, diagnosing and monitoring CKD.

A nanotechnology-based device that imitates the canine olfactory system (so-called **NA-NOSE**) and analyze the **exhaled breath** of people for screening, diagnosing and monitoring various diseases and discriminate between the different stages of the disease.

[9] ACS (ASAP); *Nature Nanotechnology* **4**, 669-673 (2009); NanoLetters **9(4)**, 1362-1368 (2009); *ACS NANO*, **3(5)**, 1258-1266 (2009) ;& Nanoletters **8(11)**, 3631-3635 (2008)

Fig. 2 The Methodology

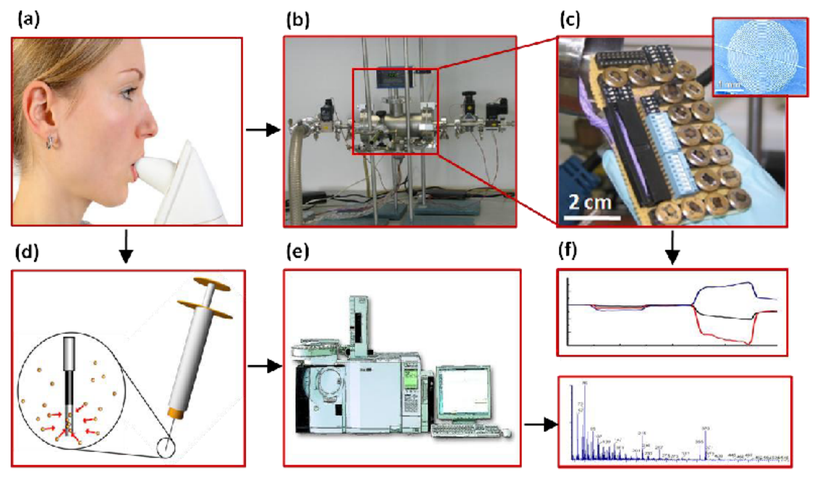
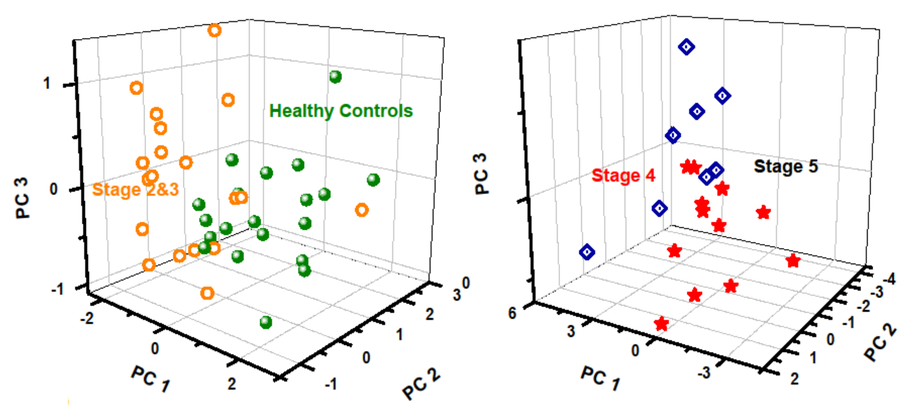


Illustration of the experimental procedure that will be used in the proposed research. **(a)** Collection of alveolar breath; **(b)** the breath sample is fed into an exposure cell; **(c)** an array of cross-reactive sensors (composing the NA-NOSE); **(d)** solid phase microextarction (SPME) for preconcentrating the breath sample; **(e)** GC-MS for the preconcentrated breath sample; **(f)** typical signal output from the NA-NOSE (upper figure)

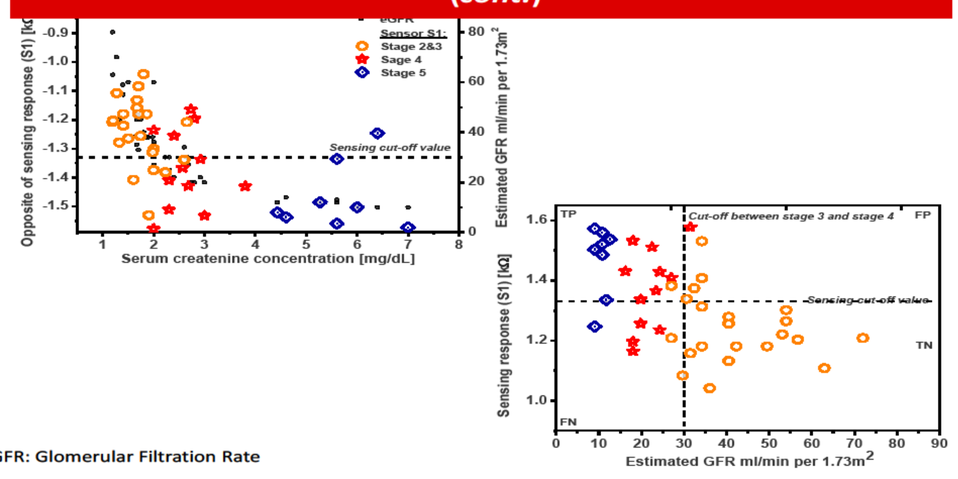
Fig.3: Analysis of CKD from Exhaled Breath – Clinical Study



	Classified as stage-2&3	Classified as healthy
Stage-2&3	17	5
Healthy	4	16

	Classified as stage-5	Classified as stage-4
Stage-5	6	2
Stage-4	1	11

Fig.4: Analysis of CKD from Exhaled Breath – Clinical Study (*cont.*)



GFR: Glomerular Filtration Rate

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