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Rapid, Diagnostic Test for Cardiac Ischemia

CLSE 203 | **Team members:** Jose Gonzales, Abdelmagid Nasreldeen, Emerson Physioc, Julio Contreras, and Evan Thoresen |**Faculty adviser:** Dr. Nastassja Lewinski | **Sponsor:** VCU Anesthesiology/Nephrology | **Sponsor adviser:** Dr. Lynne Gehr and Dr. Todd Gehr

Background

Chest pain is the second most common reason Americans visit the emergency room, which amounts to 7-8 million visits each year [1]. These visits are often because when chest pain ensues, the first thing people think is heart attack. However, several factors can cause chest pain, such as stress and panic attacks.

A heart attack, or myocardial infarction, occurs when blood flow to the heart is restricted, often by a blood clot (Figure 1). Before the onset of a heart attack, *myocardial ischemia*, which is an inadequate blood supply to the heart, can occur.

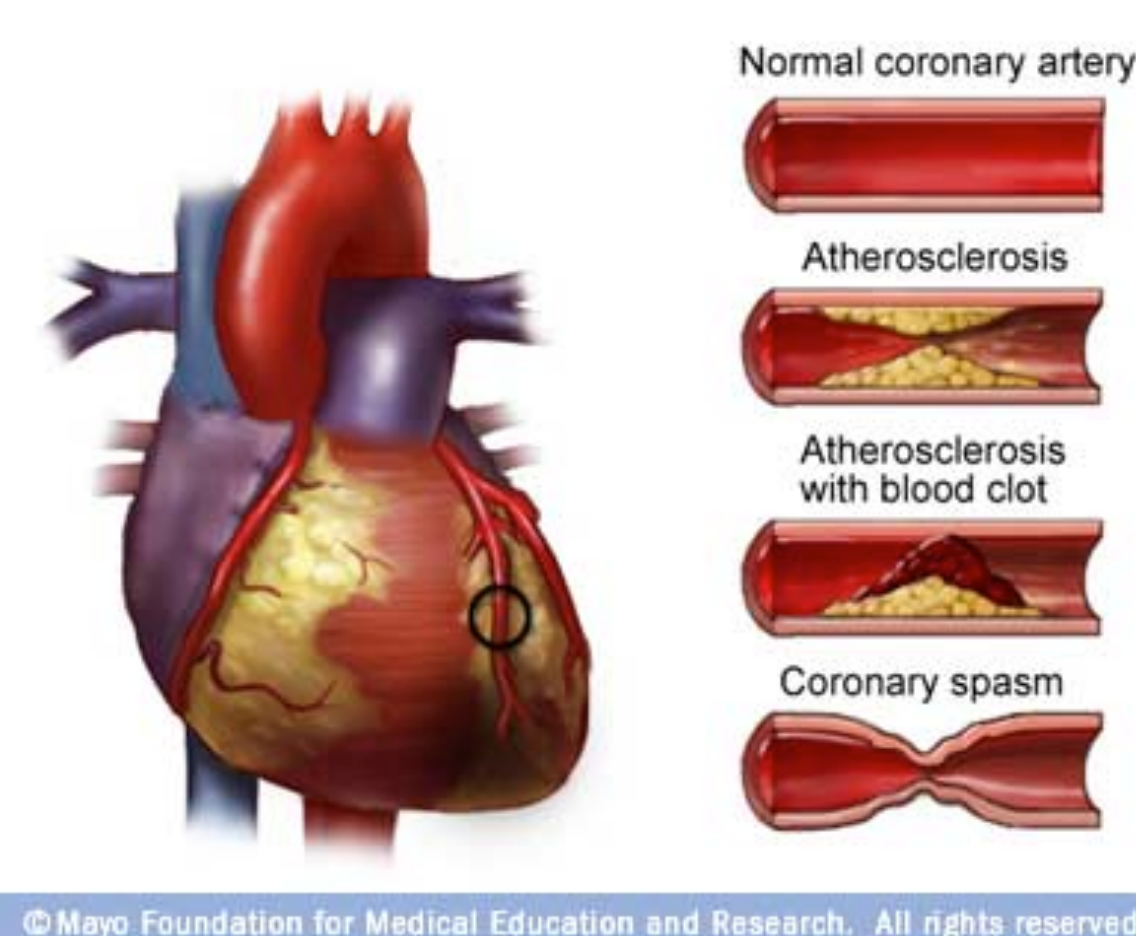


Figure 1. Coronary events that can lead to ischemia.

Problem

Current tests for myocardial infarction use the biomarker, troponin, for diagnosis. Diagnostic levels of troponin are observed *hours after the event*.

Diagnosis of infarction via troponin:

1. Prolonged myocardial ischemia
2. Myocardial infarction
3. Ambulance to ER
4. Treatment (hours wait for troponin test)
5. Confirmed diagnosis
6. Further treatment

There is a critical need for detection methods that yield much sooner diagnoses of infarction or rather possibilities of infarction.

Innovation

New Assay:

- A VCU patented chemiluminescent assay [2] uses xanthine oxidase (XO) activity in a microliter sample of blood to detect biomarkers inosine and hypoxanthine indicative of myocardial ischemia (Figure 2). Prolonged and untreated ischemia leads to infarction.
- Metabolic byproducts of XO activity is detectable within minutes of an ischemic event.

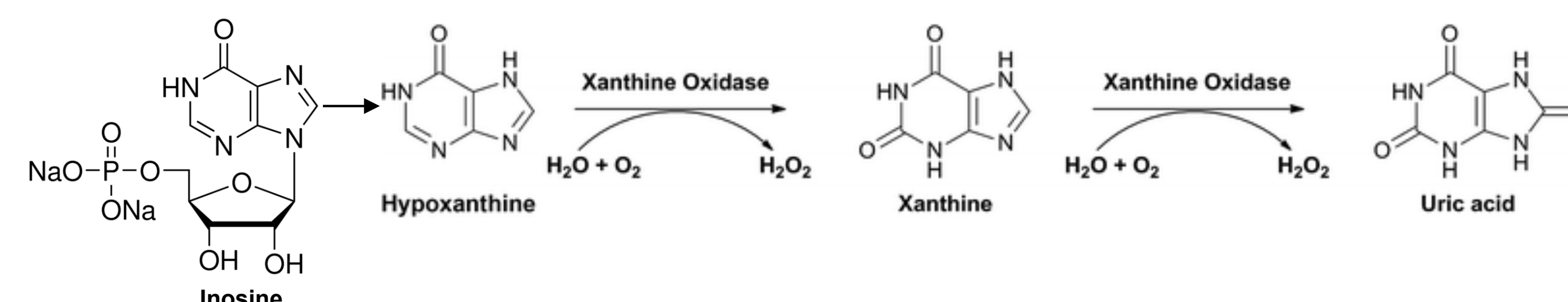


Figure 2. Principle of the chemiluminescent ischemia bioassay.

Objective:

- To build a point-of-care device to screen for cardiac ischemia using the VCU patented assay.

Design Criteria:

- Rapid (less than 10 minutes) analysis time
- Sensitive (20µL plasma sample) and specific to inosine and hypoxanthine
- Portable (handheld) device

Design Approach:

- The device will contain a multilayered microfluidic lab-on-chip (Figure 3) where the assay will be run.

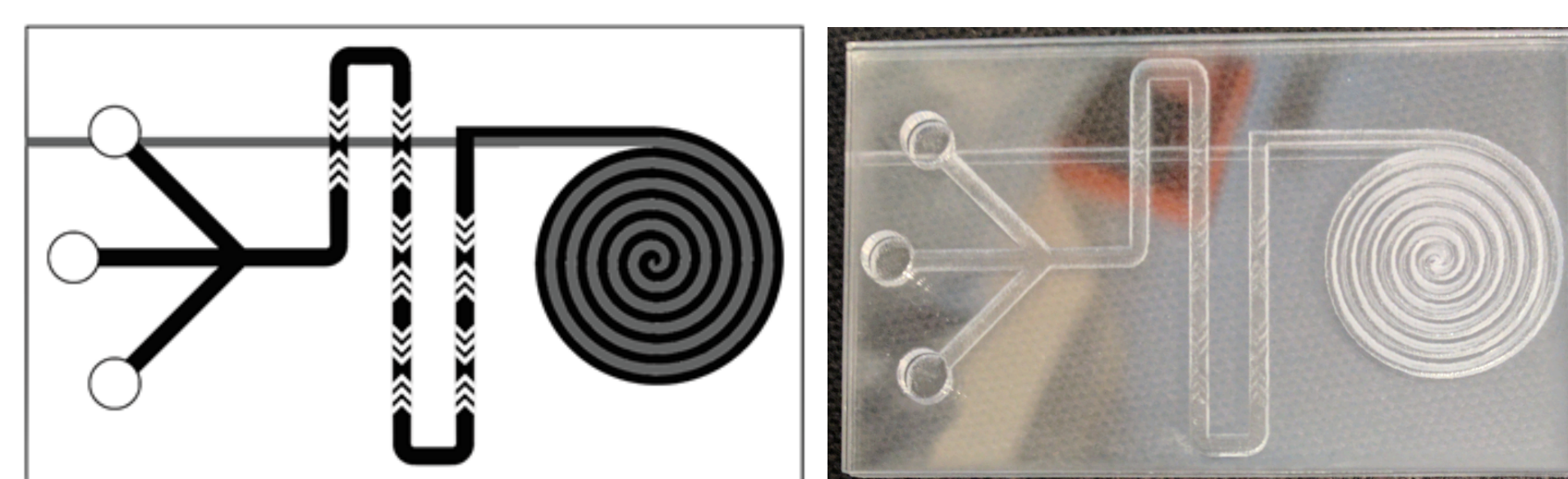


Figure 3. Top view diagram (left) and photo (right) of lab-on-chip design.

- Plasma and assay reagents enter the device through circular inlet ports. Solutions mix within micromixing channels (pleated arrow pattern). Reaction products feed into an Archimedean spiral which amplifies the chemiluminescent signal for detection using a luminometer [3].

Performance

Luminescence:

Comparing results from a single well in 12 well plate (SA = 4 cm²) to the spiral on chip (SA = 6 cm²), a 5 fold increase, as shown in Figure 4, in luminescence intensity was measured from 0.2 mL of luminol at a concentration of 24 mg/mL.

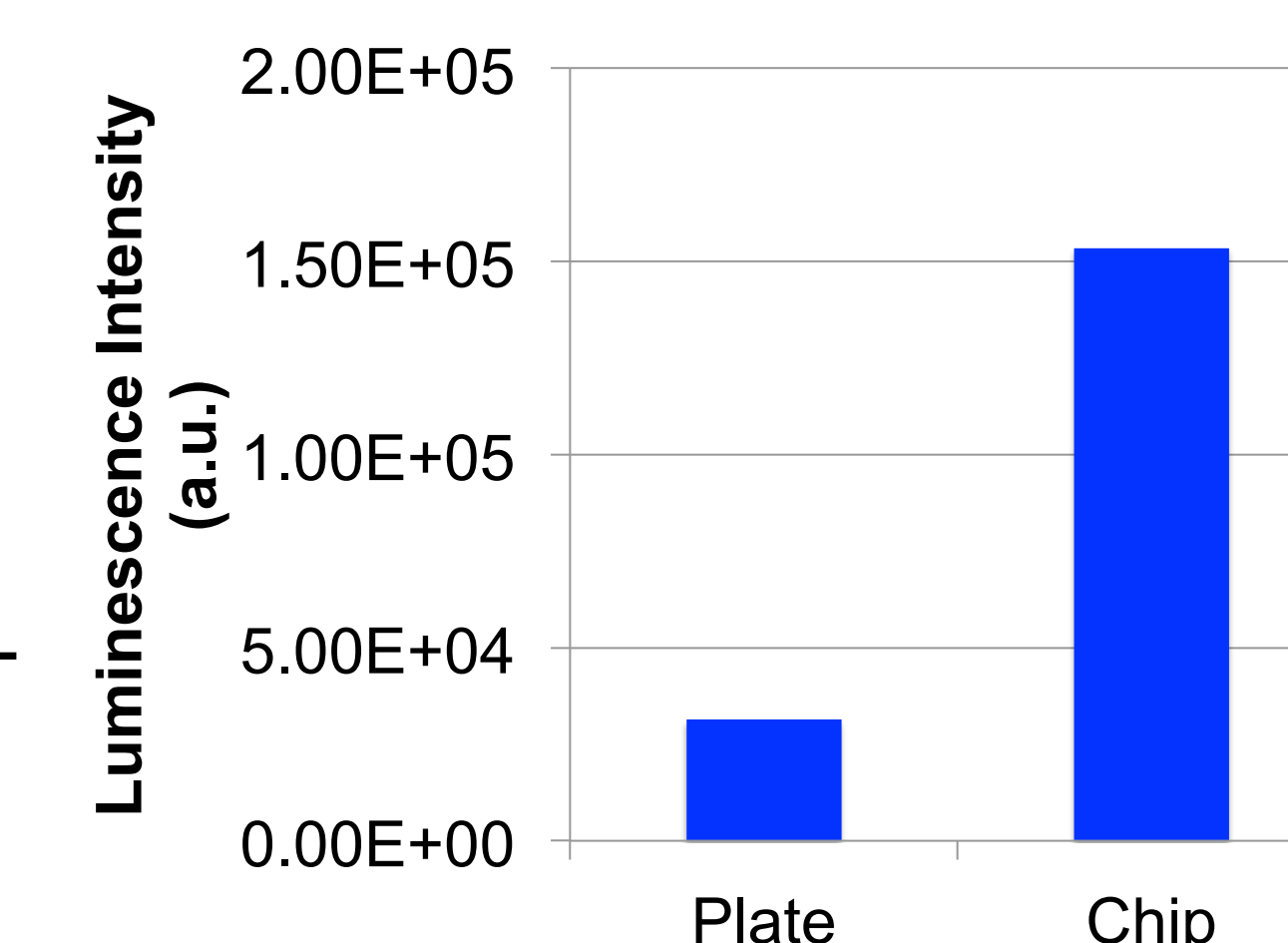


Figure 4. Luminol reading from 12 well plate and lab-on-chip.

Future Improvements

- Installing a system to separate plasma from whole blood.
- Installing a system to include prepared reagents.
- Optimizing channels for better mixing and incubation times.
- Reverse engineering a portable luminometer to detect chemiluminescence on the LOC.
- Installing a digital display to output YES or NO result.

Potential users:

- Hospital/clinic personnel
- Emergency Medical Services (EMS) personnel
- Patients testing at home

Acknowledgements

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References

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- [2] Farthing D, Xi L, Karnes HT, Sica D, Gehr T, Gehr L, Unverdorben M. "Method for diagnosing acute cardiac ischemia." U.S. Patent 8,343,731, 2013.
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