Enhancing the Design and Consistency of an α-particle Irradiator for In Vitro Experiments

Benjamin Kohler, Marco Tulio Reis, Poliana Marinello, Gabriel Sawakuchi
The University of Texas MD Anderson Cancer Center, Houston, Texas
Michigan State University, East Lansing, Michigan

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Introduction

Radiation therapy employs various radiation forms with different capacities to impact DNA within cells. This depends on their linear energy transfer (LET), which measures the energy deposited by ionizing radiation per unit length of tissue. High-LET α-particles (70-200 keV/µm), are effective in inducing clustered DNA lesions, resulting in higher cell kill and immunostimulatory effects [1]. However, delivering α-particles to the entire solid tumor volume through conventional brachytherapy is challenging due to limited range (<90 µm in water). Diffusing α-Emitters Radiation Therapy (DaRT) addresses this by using interstitial cylindrical seeds coated with radium-224, which extends α-particles' range by utilizing a unique decay chain, including radon-220. This allows α-particles to deposit doses over 2-3 mm from the seed [2]. In 2D cultures, achieving consistent dosimetry with DaRT is challenging due to the geometry of the seeds, causing a rapid dose rate decline. To overcome this, a specialized α-particle irradiator was designed, utilizing an Americium-241 (Am-241) source to provide controlled and predictable exposure. Improving on this, a shutter system was incorporated to block and expose α-particles at desired time-points, creating an efficient system for consistent and accurate α-particle exposure during in vitro experiments.

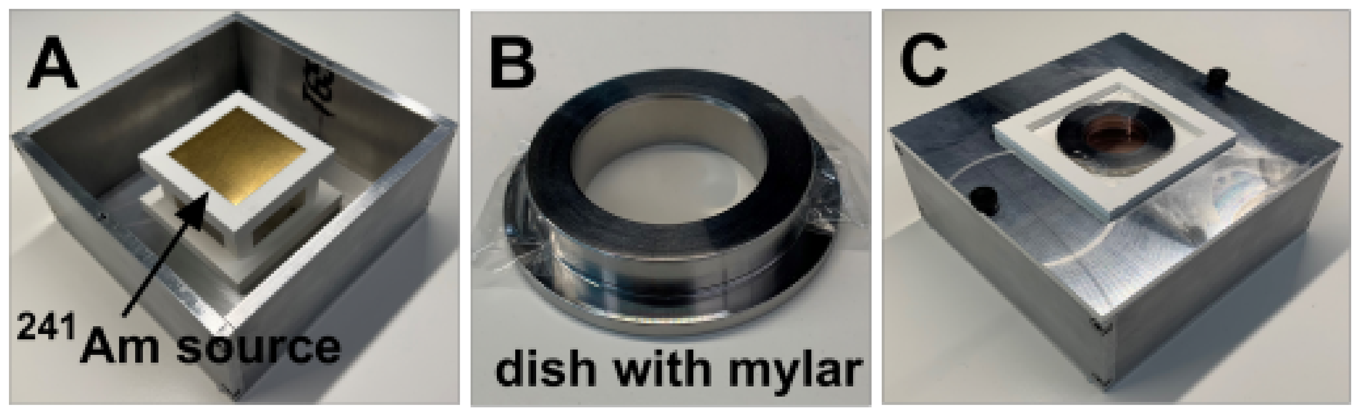

Figure 1. Components of the α-particle irradiator before the addition of a shutter. Photo A depicts the α source, B shows the cell dish with mylar to adhere to, and C is the complete assembly.

Methods

Solenoid Actuation: To test the controlled shutter movement, a high-performance solenoid (DSRS-0640-26-45D) was employed. The solenoid was activated using an Arduino Uno micro-controller, which was programmed to generate a small signal pulse to the BTS7960 power motor, functioning as an H-bridge driver circuit. This configuration allowed the full voltage to pass through, powering the solenoid to induce the desired shutter movement.

Arduino IDE Code: The code defines pins to interface with the BTS7960 motor driver and the motor. It uses a library to simplify interaction with the motor driver, providing predefined functions for motor rotation and speed control. Initialization is done in setup(), and in loop(), various motor control operations are performed, including rotation in both clockwise and counterclockwise directions with different speeds and delays.

3D CAD Enclosure: The physical integrity and protection of the sensitive components were achieved through a custom-designed enclosure manufactured using 3D CAD software (Autodesk Fusion 360). The utilization of advanced design software enabled precise measurements, intricate detailing, and the creation of a robust casing to house the solenoid, Arduino Uno, BTS7960 motor driver, and associated circuitry.

Results

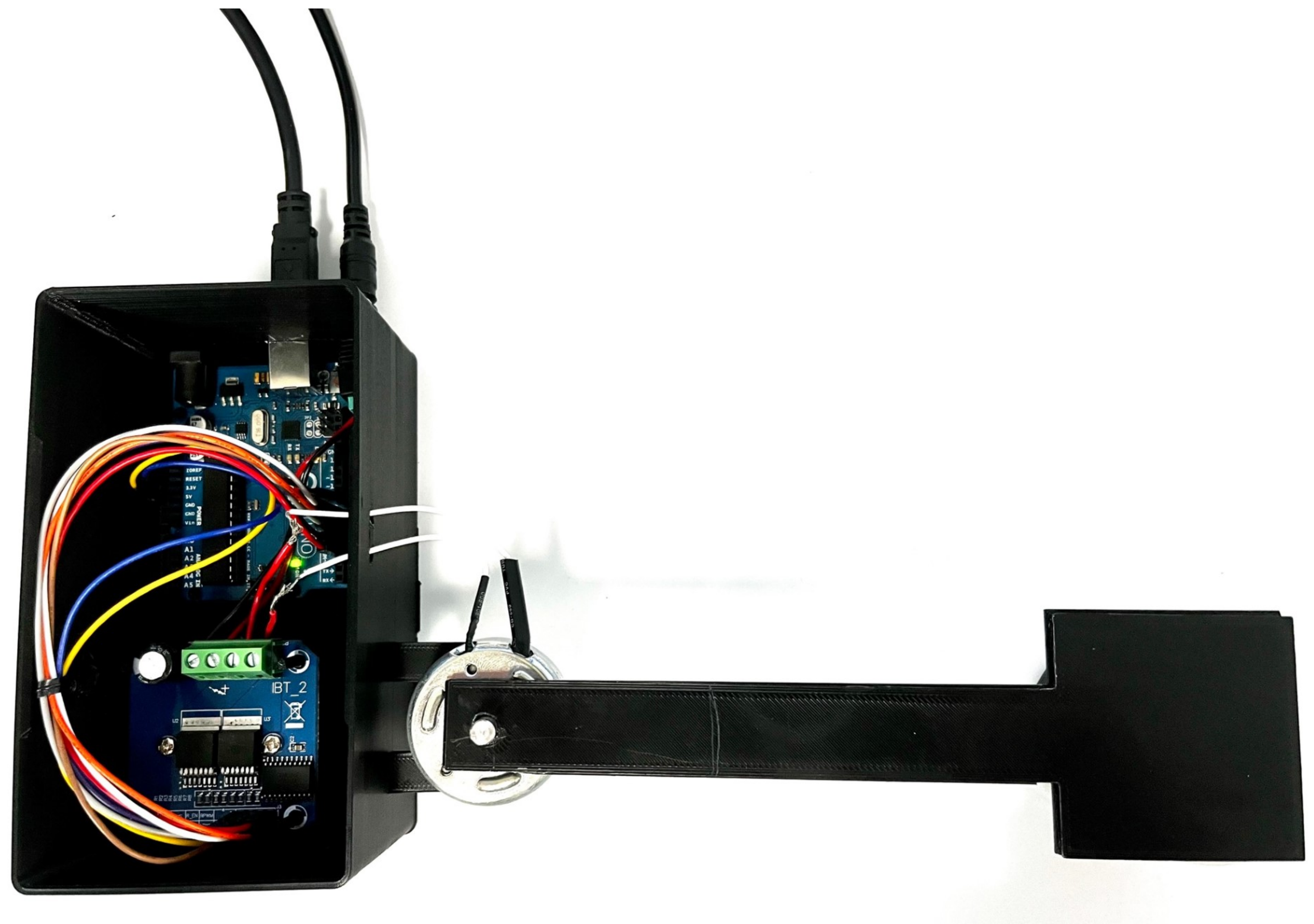

Figure 2. Solenoid shutter system controlled with an Arduino Uno and BTS7960)

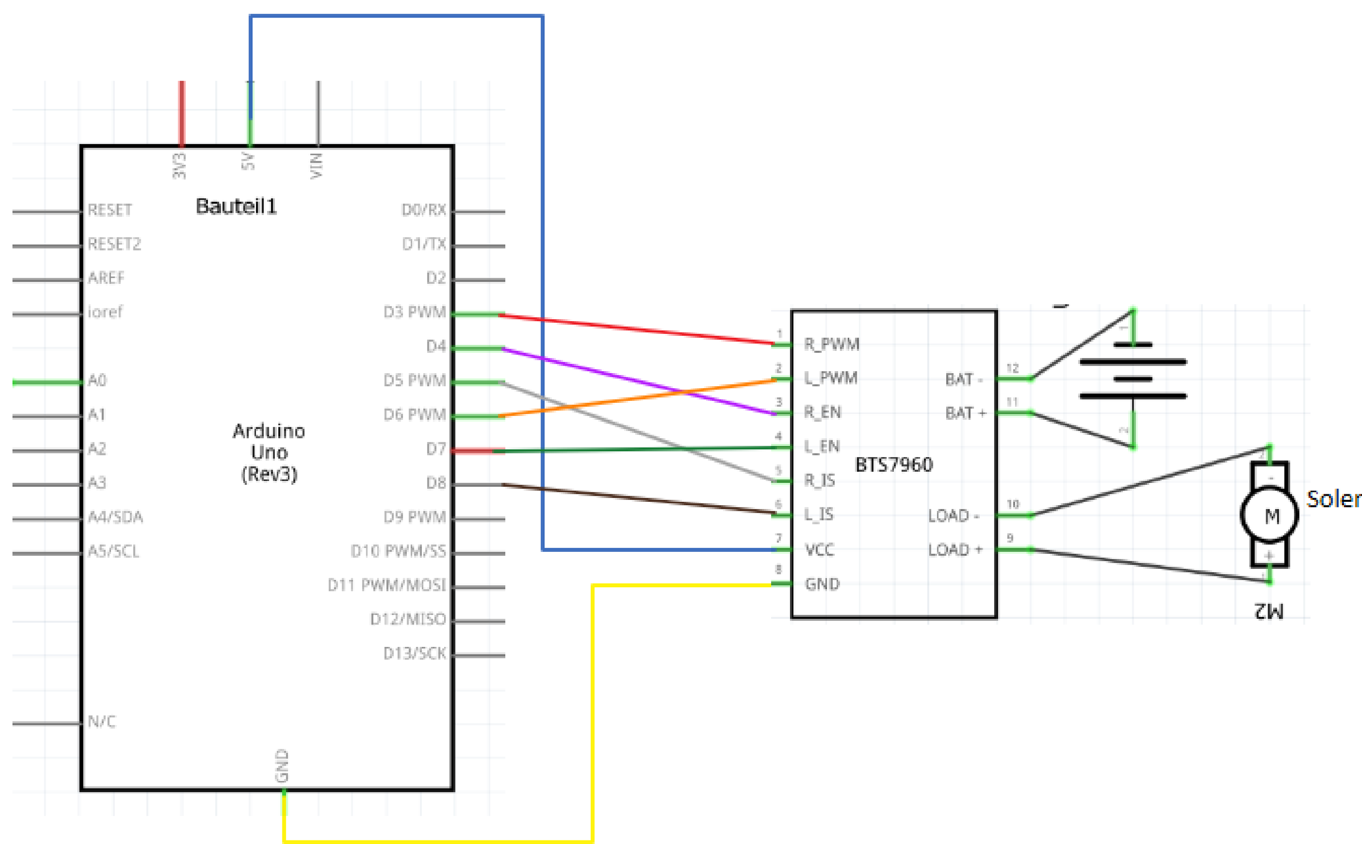

Figure 3. Circuit diagram for the system including the solenoid, arduino, BTS7960, and power source (24V)

Arduino-Control-Code.ino

```
#define RPWM 3 // define pin 3 for RPWM pin (output)
#define R_EN 4 // define pin 2 for R_EN pin (input)
#define R_IS 5 // define pin 5 for R_IS pin (output)

#define LPWM 6 // define pin 6 for LPWM pin (output)
#define L_EN 7 // define pin 7 for L_EN pin (input)
#define L_IS 8 // define pin 8 for L_IS pin (output)
#define CW 1 //do not change
#define CCW 0 //do not change
#define debug 1 //change to 0 to hide serial monitor debugging information or set to 1 to view

#include <BTS7960.h> //downloads BTS7960 library from desktop
BTS7960 motor(R_EN,RPWM,R_IS, L_EN,LPWM,L_IS,debug);

void setup() {
  Serial.begin(9600);// setup Serial Monitor to display information

   motor.begin();
}

void loop() {
    motor.rotate(100,CW);// run motor with 100% speed in CW direction
    delay(2000);//run for 5 seconds
    motor.stop();// stop the motor
      while (true) {
    // This loop will keep the program stuck here after stopping the motor
    // The program will not enter the motor.rotate() and delay() again.
  }
}
```

Figure 4. Arduino IDE code written to control the solenoid for a specified time period

Discussion

One of the primary objectives of this study was to improve the accuracy of dosimetry delivery by implementing a reliable shutter system. The utilization of a high-performance solenoid, driven by the Arduino Uno microcontroller, demonstrated the feasibility of achieving controlled and precise shutter movements. The combination of the BTS7960 power motor allowed for seamless interfacing with the Arduino Uno, facilitating full voltage delivery to the solenoid. As a result, the shutter system demonstrated robust and consistent performance, eliminating potential errors associated with manual interventions and leading to improved dosimetric accuracy during radiation exposure

Further Work

Some critical aspects need attention before declaring the irradiator complete, such as addressing power consumption and heating issues by using a higher-quality solenoid with reduced voltage requirements. Additionally, incorporating a collimator could enhance dosimetry precision, leading to more sophisticated in vitro experiments. Despite the current limitations, this work lays a solid foundation for ongoing improvements to α irradiators, showcasing dedication and ingenuity in the pursuit of enhanced radiation delivery systems for in vitro experimentation.

References

1. Bonaventura P, Shekarian T, Alcazer V, Valladeau-Guilemond J, Valsesia-Wittmann S, Amigorena S, Caux C, Depil S. Cold Tumors: A Therapeutic Challenge for Immunotherapy [published online ahead of print 2019/02/26]. Front Immunol. 2019;10:168.

2. Popovtzer A, Rosenfeld E, Mizrachi A, Bellia SR, Ben-Hur R, Feliciani G, Sarnelli A, Arazi L, Deutsch L, Kelson I, Keisari Y. Initial Safety and Tumor Control Results From a "First-in-Human" Multicenter Prospective Trial Evaluating a Novel Alpha-Emitting Radionuclide for the Treatment of Locally Advanced Recurrent Squamous Cell Carcinomas of the Skin and Head and Neck. International Journal of Radiation Oncology*Biology*Physics. 2020;106(3):571-578.

Acknowledgments

This Research was partially funded by Alpha Tau Medical, Radiation Oncology Strategic Initiatives from MD Anderson Cancer Center, and NCI (RO1CA279119-01).