HSLU Hochschule Luzern

Technik & Architektur
Master's Thesis MSE Medical Technology

Master's Thesis MSc FHZ in Engineering with Specialization in Medical Technology

Investigation of Surrogates and Models of Human Whole Blood for Hematology Applications

Figure 1: Main steps of the cobas m 511 including the printing of a monolayer of cells, staining and imaging. Source: Roche Diagnostics International Ltd.

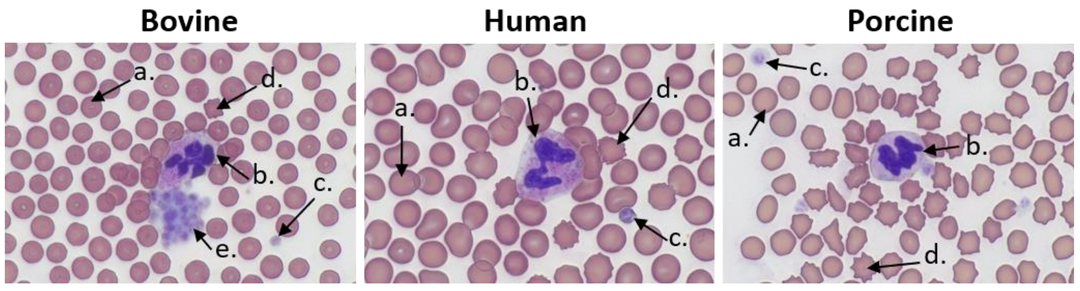

Figure 2: Cobas m 511 exemplary sample images for bovine, human & porcine blood with highlighted blood cell examples for a. Red blood cells, b. White blood cells, c. Platelets, d. Echinocytes & e. Platelet clumps.

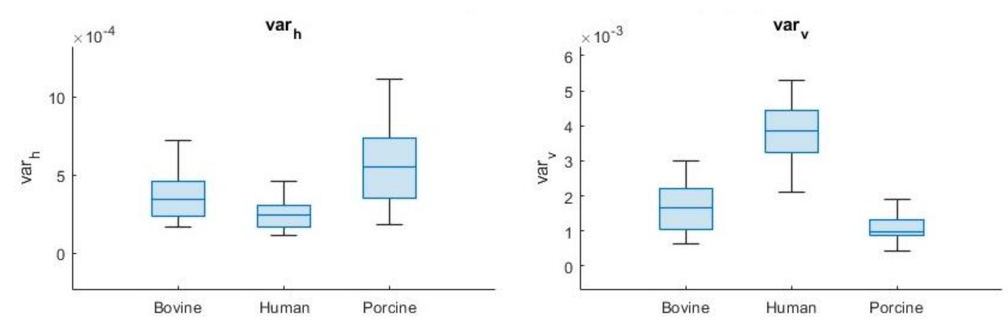

Figure 3: Printing quality was evaluated based on the variations in cell coverage in horizontal (var_h) and vertical (var_v) directions. Var_v measures differences between the central region and the edges of the print. Var_h measures differences from the start to the end of the printing process. Horizontal variation in direction of cell deposition i.e. printing was larger for animal blood, vertical smaller.

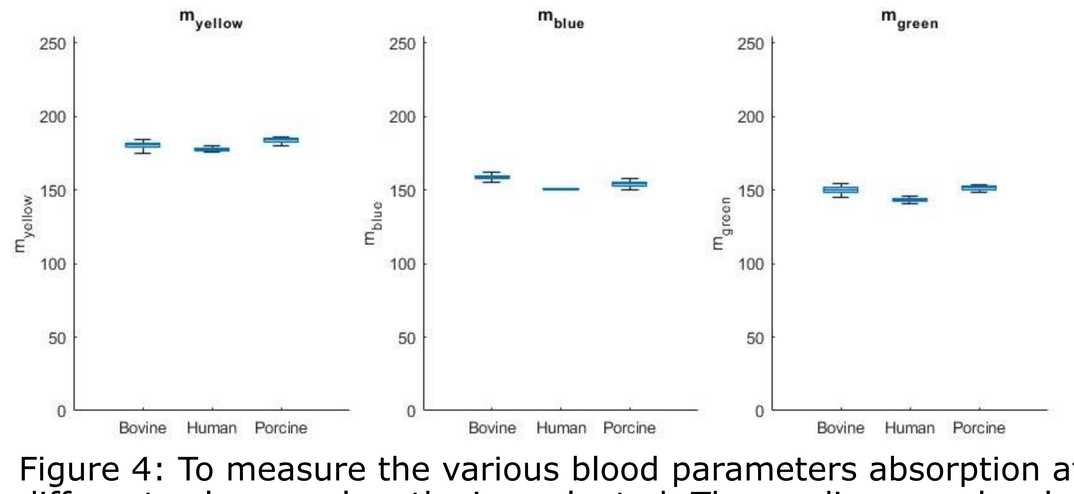

Figure 4: To measure the various blood parameters absorption at different color wavelengths is evaluated. The median grey levels of the yellow (m_{yellow}), blue (m_{blue}) and green (m_{green}) colors are in the same range for all three species, indicating that the overall stain intensity is similar for bovine, porcine, and human prints.

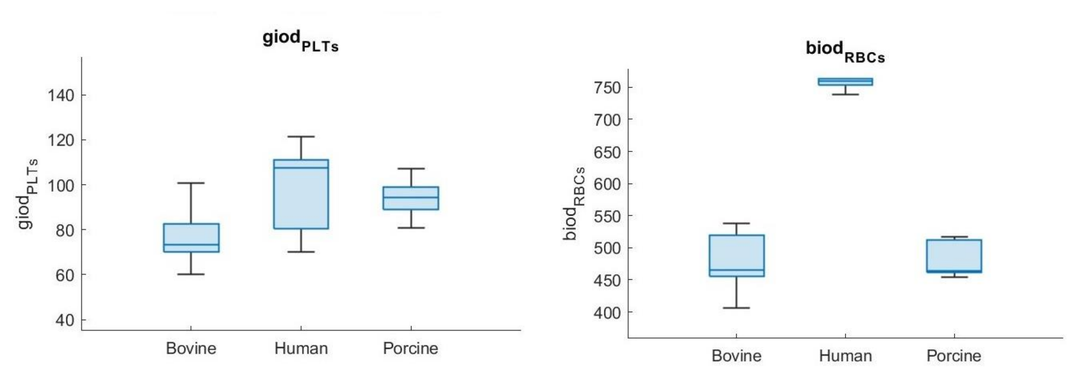

Figure 5: The integrated optical density (absorbance) was analyzed using the green color for the platelets ($giod_{PLTs}$) and the blue color for the red blood cells ($biod_{RBCs}$), since that is were absorbance and thus contrast is max. for those cells. Absorbance of the platelets was similar for all species, whereas absorbance of the red blood cells was higher for human compared to bovine and porcine blood. These differences can be explained by higher hemoglobin levels and a larger cell volume.

Project Assignment & Aim

The development of medical devices is heavily reliant on the supply of human blood samples. Human blood is, however, of limited supply and relies on donors. This project aimed to evaluate the feasibility of using livestock animal blood, as surrogates for human whole blood in development activities of medical devices in the field of hematology.

Methods

Rheological and morphological characteristics of blood were investigated through a literature review, with focus on bovine, porcine, ovine, and avian blood. Printing i.e. cell monolayer creation on a glass slide & staining quality and blood parameters of bovine and porcine blood were measured on the cobas m 511 (Roche Diagnostics International Ltd., Rotkreuz, Switzerland) and compared to human blood. The cobas m 511 is a fully integrated hematology analyzer that prints a monolayer of blood, stains, images and analyzes it (Fig. 1). Additionally, the flow behavior during the printing process was inquired conducting flow rate measurements of blood flow rate during sample processing on the device.

Results & Discussion

The literature showed that blood properties vary widely for all investigated species. In terms of composition and properties, porcine blood was the most similar to human. Figure 2 shows sample images. Further, the results showed that animal blood could be printed (Fig. 3) and stained (Fig. 4-5) similarly to human blood, with the majority of differences being artifacts of different cell sizes. However, there were issues with platelet clumping, possibly due to anticoagulation using ethylene diamine tetra acetic acid or pre-analytical error. Moreover, porcine blood showed a high number of echinocytes. This can, however, be natural for pigs. The flow rate measurement results suggest that porcine blood is the better surrogate for human blood in terms of viscosity and visco-elastic effects. Sample age and storage condition have a similar influence on animal blood as on human blood.
Overall, the study suggests that bovine and porcine blood can be used as surrogates for human blood in hematology development activities of medical devices.

Still, it is important to consider limitations and establish historical values for these blood types before detection of deviations in medical device processes can be achieved.

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