



Morphometric traits to estimate brain and liver weight and their ratio for the diagnosis of intrauterine growth restriction in newborn piglets



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ABSTRACT

Intrauterine growth restriction (IUGR) is defined as inadequate foetal growth during gestation. In response to placenta insufficiency, IUGR piglets prioritise brain development as a survival mechanism. This adaptation leads to a higher brain-to-liver weight ratio (BrW/LW) at birth. This study assessed the potential of using morphometric traits to estimate brain (BrW) and liver (LW) weights, enabling non-invasive diagnosis of IUGR in newborn piglets. At birth, body weight (BtW) of individual piglets ($n = 144$) was recorded. One day (± 1) after birth, BrW and LW were measured with computed tomography ($n = 94$) or by weighing the organs after natural death or euthanasia ($n = 50$). Additionally, 20 morphometric traits were captured from images of each piglet and correlated with the BrW and LW. The morphometric traits that showed a $r \geq 0.70$ in linear correlation with the BrW or LW were selected. Each selected trait was combined as an independent variable with BtW to develop multiple linear regression models to predict the BrW and LW. Six models were chosen based on the highest adjusted R^2 value: three for estimating BrW and three for LW. The dataset was then randomly divided into a training (75% of the data) and a testing (remaining 25%) subsets. Within the training subset, three equations to predict the BrW and three to predict the LW were extrapolated from the six selected models. The equations were then applied to the testing subset. The accuracy of the equations in predicting organ weight was assessed by calculating mean absolute and mean absolute percentage error (MAE and MAPE) between predicted and actual BrW and LW. To predict the BrW/LW, an equation including BtW and the two morphometric traits which better predicted BrW and LW was used. In the testing dataset, the equation combining ear distance and BtW better estimated the BrW. The equation performed with a MAE of 1.95 and a MAPE of 0.06 between the true and estimated weight of the brain. For the liver, the equation combining the abdominal area delimited by a square and BtW displayed the best performance, with a MAE of 9.29 and a MAPE of 0.17 between the true and estimated weight. Finally, the MAE and MAPE between the actual and estimated BrW/LW were 0.14 and 0.17, respectively. These findings suggest that specific morphometric traits can be used to estimate brain and liver weights, facilitating accurate and non-invasive identification of IUGR in newborn piglets.

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Implications

Selection to improve sows' prolificacy has led to an increased percentage of piglets exposed to intrauterine growth restriction. This condition is characterised by a relative increase in brain size compared with other organs, such as the liver. Therefore, the diagnosis should consider the ratio between the weight of the brain and that of other organs. Our study shows that there are morphometric traits which can be used to estimate brain and liver weight in newborn piglets. Predictive models based on these traits repre-

sent a promising tool for the early detection of affected piglets, enabling the development of targeted postnatal interventions.

Introduction

Efforts to improve sows' prolificacy have led to a significant increase in the number of piglets born and weaned per year (Quiniou et al., 2002; Campos et al., 2012). Although litter sizes have increased, not all piglets born in these larger litters attain their full genetic growth potential. This can be attributed to an increased exposure to growth restrictions experienced in the uterine environment (Quiniou et al., 2002; Amdi et al., 2013). Intrauter-

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ine growth restriction (**IUGR**) is a pathological condition characterised by impaired development of the foetus or its organs during gestation (Wu et al., 2006). The primary cause behind IUGR is placental insufficiency, which results in inadequate distribution of oxygen and nutrients to the foetus (Cohen et al., 2015). Intrauterine growth restriction is associated with increased morbidity and mortality, long-term growth limitation, and low efficiency in nutrient utilization (Wu et al., 2006). At present, this condition represents the main cause of low birth weight (**BtW**) in the pig industry and can affect up to 20% of piglets within a litter (Santos et al., 2022). The identification of IUGR piglets is challenging due to the lack of specific symptoms and reliable biomarkers. Diagnosis is frequently established by considering either the absolute BW of the foetus or newborn or the BW in relation to a specific gestational age (Van Ginneken et al., 2023). D'Inca et al. (2010) classified piglets as IUGR when their BtW was at least 1.5 SD units lower than the average BtW of the litter. Other studies have defined IUGR as weighting at birth less than the tenth percentile of gestational age-specific normal BtW values (Bauer et al., 2003). In a study by Wang et al. (2016), an IUGR piglet was defined as having a BtW between 0.75 and 0.90 kg and belonging to the lower quartile of the litter BtWs. However, it is important to differentiate between the definitions of IUGR, low BtW, and 'small for gestational age'. These terms are often used interchangeably but have important differences, as they each represent a distinct aspect of foetal growth and development (Gupta, 2008). Indeed, within the low BtW and small for gestation age categories, there are subjects that do not achieve their full genetically determined size because of growth restriction in the uterus (De Vos et al., 2014). It has been suggested that in order to identify IUGR piglets, it is important to consider their head morphology as an additional criterion (to BtW) (Hales et al., 2013). Moreover, Huting et al. (2018) demonstrated that the morphology of a newborn piglet may also be useful in predicting its later performance. Piglets that suffered from growth restriction in the uterus often show a dolphin-like head shape, wrinkles perpendicular to the mouth, bulging eyes, and hair with no direction of growth (Hales et al., 2013; Amdt et al., 2020). Besides these phenotypical traits, IUGR has been associated with a relatively larger brain compared to other organs at birth, such as the liver. Due to the oxygen and nutrient deprivation during foetal growth, development of the brain is prioritized. This survival mechanism is called the "brain-sparing effect" and results in a higher brain-to-organ weight ratio at birth (Cohen et al., 2015). For this reason, to accurately assess IUGR in newborn piglets, measurements like BtW and head shape should be complemented by evaluating the proportional relationship between brain weight (**BrW**) and the weight of other organs (Chand et al., 2022; Felicioni et al., 2019). The absence of a non-invasive method to assess this ratio and diagnose IUGR remains a significant challenge in pig production, limiting treatment development due to poor diagnosis (Felicioni et al., 2019). Considering the adverse effects of IUGR on pig production and the inconsistencies in studies on growth-restricted pigs, there is a clear need for an accurate and standardized diagnostic approach. Models based on image analysis offer a promising tool for the early and non-invasive identification of IUGR in piglets, facilitating interventions to mitigate its negative effects.

Our hypothesis was that using specific morphometric traits, the weight of the brain, that of the liver (**LW**), and their ratio (**BrW/LW**) could be estimated with sufficiently high accuracy, enabling non-invasive diagnosis of IUGR in newborn piglets. To test this hypothesis, we determined the weight of the brain and liver in newborn piglets through either scale measurement after natural death or euthanasia or by extrapolation from computed tomography (**CT**) scan images. In addition, pictures of the same piglets were taken to capture specific body measurements such as distance between

the ears, body length, and front head diameter, which were used to predict the BrW, LW, and BrW/LW.

Material and methods

Animal selection and classification

The study was approved (approval numbers 32751_FR and 35131_FR) by the ethics committee of the canton of Fribourg (Switzerland). The experiment was performed at the Agroscope swine research facility situated in Posieux (Switzerland). Two studies were carried out. In the first study, 310 Swiss Large White piglets (alive = 268, stillborn/dead = 42) were included. The BtW of each piglet was registered on the day of farrowing (day 0). The BtW of the piglets born during the evening or night was measured the following morning. One day (± 1) after birth, CT scan imaging (64-channel multislice scanner Siemens Emotion Duo CT, Siemens, Erlangen, Germany) was conducted to non-invasively measure brain and liver volumes for each piglet. The procedures for handling the pigs and analysing the CT scan images were described in detail by Ruggeri et al. (2024). Briefly, all the animals were anaesthetized with isoflurane and positioned in sternal recumbency for CT scans of the head and the thoracic region. The resulting images were then semi-automatically processed (Turtleseg software 1.2.1) to calculate the volumes of the brain and liver. After the CT scan, 30 piglets were selected and euthanised with an intracardiac injection of pentobarbital solution (Esconarkon, Streuli Tiergesundheits AG, Uznach, Switzerland), as described by Ruggeri et al. (2024). The selection was based on the BtW. Three BtW categories were defined to include the full range of BtWs present in the study population. From each category, 10 piglets were euthanised. The brain and the blood-filled liver were excised. Brain (**BrW_{Eu}**) and liver (**LW_{Eu}**) weights were assessed with a scale, and their volumes were determined using the water displacement method (Lemke et al., 2006). Volume and weight were used to calculate the density of the brain and liver according to Equations 1 and 2 (Annex 1).

The average brain and liver densities calculated post-euthanasia together with the brain and liver volumes measured with the CT scan were used to assess brain weight (**BrW_{CT}**), liver weight (**LW_{CT}**), and the brain-to-liver weight ratio (**BrW_{CT}/LW_{CT}**) for all the piglets. In order to estimate the weights of the brain and liver from CT scan images, it is essential to have the information about the densities of these organs. We hypothesized that densities of the brain and liver are comparable among piglets and estimated them using the average densities from euthanised piglets. The BrW_{CT} and LW_{CT} were then calculated according to Equations 2 and 3 (Annex 1).

Furthermore, using the data obtained from the 30 euthanised piglets, three regression equations were developed with Python programming language (version 3.8.8) to calculate the BrW_{CT}, LW_{CT}, and BrW_{CT}/LW_{CT} from the weights obtained after death/euthanasia (BrW_{Eu}, LW_{Eu}, BrW_{Eu}/LW_{Eu}).

To extend the dataset, which was unbalanced due to the limited number of piglets exhibiting a high BrW_{CT}/LW_{CT} compared to the population mean, a second experiment was performed at the same facility.

All Swiss Large White piglets born from 35 litters with a BtW lower than 1 kg were included (n = 67, alive = 35, stillborn/dead = 32). On the day of farrowing (day 0), the BtW of each piglet was recorded. The BtW of the piglets born during the evening or night was measured the following morning. On day one (± 1) after birth, the piglets (n = 35) were euthanised with an overdose of pentobarbital (Esconarkon). The brain and blood-filled liver were then excised from each piglet (alive = 35, stillborn/dead = 32), as

described before. The BrW_{Eu} and LW_{Eu} were assessed with a scale and used to determine the BrW_{Eu}/LW_{Eu} . As the CT scan was not available in this second study, the three regression equations developed in the first study were used to calculate the BrW_{CT} , LW_{CT} , and BrW_{CT}/LW_{CT} from the weights obtained after death/euthanasia (BrW_{Eu} , LW_{Eu} , and BrW_{Eu}/LW_{Eu}). The objective was to standardize the data of the two experiments.

Image collection and body measurements

To capture specific morphometric traits, videos of all the piglets (first study = 310, second study = 67) were recorded on day one (± 1) using a camera (RealSense depth camera D435i, Intel, USA) placed at 40 cm from the animal. Each piglet was positioned in a hammock and a short (~ 2 s) video was recorded, with the camera moving from the right lateral side to the top of the piglet. A fixed distance between the camera and the piglet was maintained thanks to a pivoting arm. Videos were then saved in BAG format. From each video, a series of individual RGB images (RGB frame resolution: $1\,920 \times 1\,080$) were extracted one by one to create a collection of frames (RGB frame rate: 30 fps). The frame extraction procedure was performed using Python programming language (version 3.8.8). The frames were then converted into PNG format through the `rs-convert.exe` tool, available within the Intel RealSense program (SDK 2.0, Intel Corporation, USA).

Body measurements were collected from frames of 144 piglets, 94 from the first study and 50 from the second study. The piglets were selected randomly, with a target total of 150, including 100 piglets from the first study and 50 from the second study, given to the latter's smaller dataset. However, six piglets from the first study were subsequently excluded because of the poor quality of their images.

Two image frames were selected for each piglet. The first frame (frame 1) shows the piglet from the right lateral side and the second (frame 2) from the top (Fig. 1). Specific measurements were taken on the frames by using ImageJ software (version 1.53, U.S. National Institutes of Health, Bethesda, Maryland, USA). For each piglet, 20 body measurements were recorded in total: 13 (frame 1: ME, pixel; MH, pixel; ME2, pixel; EH, pixel; EH2, pixel; MN, pixel; A, °; B, pixel²; frame 2 = EE, pixel; EE2, pixel; FH, pixel; Bt, pixel²; CB, pixel²) to correlate to the weight of the brain (Fig. 2), 6 (frame 1: L, pixel²; L2, pixel²; CL, pixel²; frame 2: SS, pixel; SS2, pixel; Lt, pixel²) to the weight of the liver (Fig. 3), and 1 (frame 2: Le, pixel) to both the organs' weights (Fig. 2 and Fig. 3). To test the repeatability of the method, a subset of the morphometric traits ($n = 12$) was measured on the selected piglets ($n = 144$, 94 from study one and 50 from study two) by a second observer.

Data analysis

All calculations and statistical analyses were performed using Python (version 3.8.8). The packages employed were `numpy`, `pandas`, `seaborn`, `matplotlib`, `scipy`, `scipy.stats`, `statsmodels.api`, `statsmodels.formula.api`, `sklearn.model_selection`, and `sklearn.metrics`.

The BtW and body measurements of each selected piglet ($n = 144$, 94 from study one and 50 from study two) were used to correlate with the BrW_{CT} and the LW_{CT} . The linear relations of the BtW and each morphometric trait (shown in Fig. 2 and Fig. 3) with the BrW_{CT} and LW_{CT} were tested, and the degrees of correlation were expressed as r . The morphometric traits which correlated with a $r \geq 0.70$ with either brain or liver weight were selected for further analysis. In addition, each morphometric trait was used, in combination with the BtW, as an independent variable to develop multiple linear regression models to predict the BrW_{CT} and LW_{CT} . Among the resulting models, the six morphometric traits – three

to correlate with the brain and three to correlate with the liver – which, in combination with BtW, displayed the highest adjusted R^2 value (goodness-of-fit of the linear regression model) were selected. This selection process allowed the identification of the most influential variables for predicting BrW_{CT} and LW_{CT} .

Having determined these key morphometric traits, the dataset (144 piglets, 94 from study one and 50 from study two) was randomly divided into two distinct subsets: a training dataset containing 75% of the data (108 piglets, 69 from study one and 39 from study two) and a testing dataset including the remaining 25% (36 piglets, 25 from study one and 11 from study two).

Using the training dataset, three equations to predict BrW_{CT} and three additional equations to predict LW_{CT} were developed based on the six most predictive variables (as indicated by the highest adjusted R^2 derived from the multiple linear regression models). These equations were applied on the training dataset first and subsequently on the testing datasets, to assess the predictive performances of the models on unseen data. When applying these prediction equations to both, the training and testing datasets, six distinct predicted values of BrW_{CT} were obtained for each piglet, three for the training datasets and three for the testing dataset. The same results were obtained for the liver.

In order to predict the BrW_{CT}/LW_{CT} , two approaches were tested. In the first approach, the two variables which, along with the BtW, better predicted the BrW_{CT} and LW_{CT} (lower percentage error in the testing dataset) were used in combination to develop a multiple linear regression model to predict the BrW_{CT}/LW_{CT} . Prior to this analysis, a log transformation was applied to the BrW_{CT}/LW_{CT} values, as the residuals exhibited a characteristic of non-linearity. The regression equation extrapolated from the model in the training dataset was then applied to the testing dataset. In the second approach, the predicted BrW_{CT} and LW_{CT} , calculated using the previous models, were directly employed to determine the BrW_{CT}/LW_{CT} , both in the training and testing subsets. Throughout this process, the linear relation between the true and the predicted BrW_{CT} , LW_{CT} , and BrW_{CT}/LW_{CT} was always tested, and r was reported for both the training and the testing dataset.

Finally, the models' predictive performances were evaluated using the mean absolute error (MAE), the mean absolute percentage error (MAPE), the RMSE, and the RMSE % between the true and predicted BrW_{CT} , LW_{CT} , and BrW_{CT}/LW_{CT} . The coefficients of correlation and concordance were also measured. The MAE, MAPE, RMSE, RMSE %, and the coefficients of correlation and concordance were reported for both the training and the testing dataset. Additionally, the MAE, MAPE, RMSE, RMSE %, and the coefficients of correlation and concordance between the true and predicted BrW_{CT}/LW_{CT} were measured excluding from the calculation the piglets born with a BtW below 800 g, as euthanasia of these piglets is a common practice in modern swine production systems. When the BrW_{CT}/LW_{CT} was predicted according to the first approach, the correlation coefficient, MAE, MAPE, RMSE, RMSE %, and the coefficients of correlation and concordance between true and predicted BrW_{CT}/LW_{CT} were assessed after reversing the logarithmic transformation of the data. The P -value of the correlation coefficient was always tested and considered significant at < 0.05 .

The predictive ability of the BtW alone to estimate the BrW_{CT} and LW_{CT} was tested throughout the various steps of the analysis. The inclusion of BtW as the only predictor at each step provided a baseline for comparison, enabling the evaluation of how the addition of morphometric traits improved the models' performance. Simple linear regression models, incorporating only BtW, were developed to predict BrW_{CT} , LW_{CT} , and BrW_{CT}/LW_{CT} , and their performances were evaluated on both training and testing datasets. In addition, the models including BtW as sole predictor (e.g., $BrW_{CT} \sim BtW$) and the models including BtW in combination with mor-

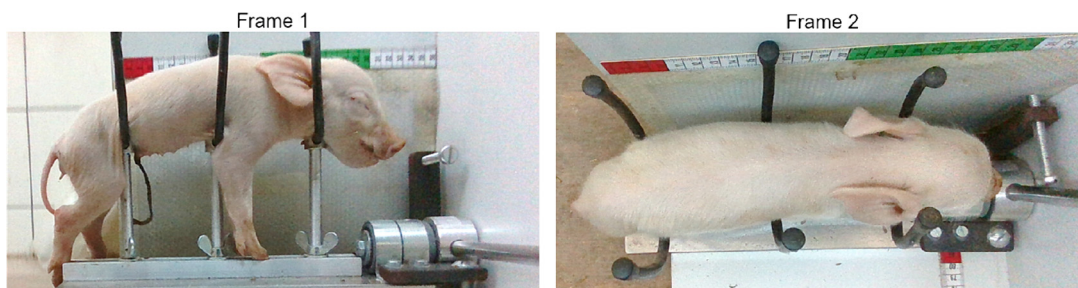


Fig. 1. Two frames were selected for each piglet to perform body measurements. Frame 1 (left) shows the piglet from the right lateral side and frame 2 (right) from the top.

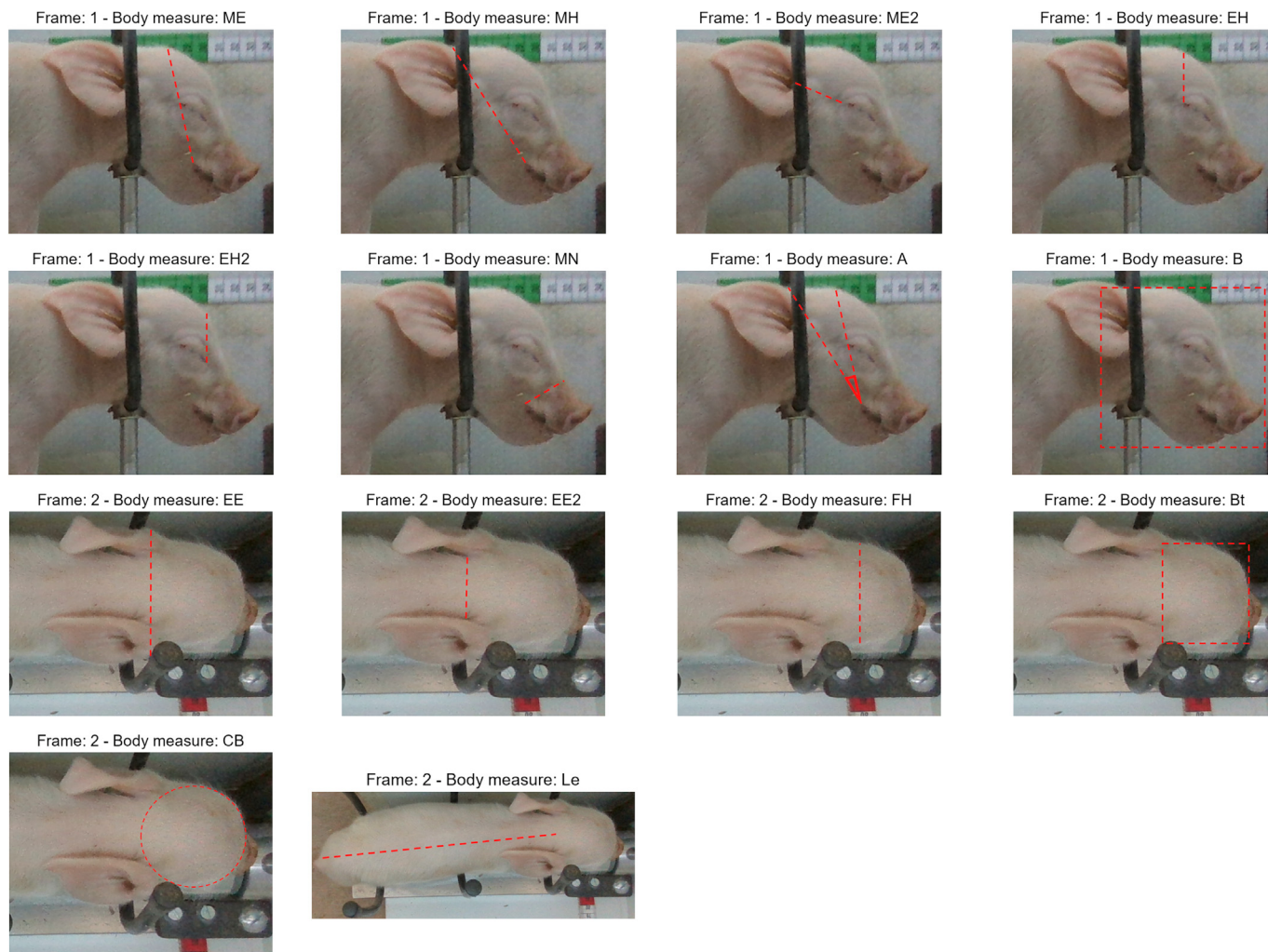


Fig. 2. Body measurements recorded to correlate with the weight of the brain of the piglets. Abbreviations: ME = distance in pixels between the mouth and the front head passing by the lateral edge of the eye, seen from the side; MH = distance in pixels between the mouth and the front head passing by the medial edge of the ear, seen from the side; ME2 = distance in pixels between the caudal edge of the eye and the ear, seen from the side; EH = distance in pixels between the lateral edge of the eye and the front head, following a straight line, seen from the side; EH2 = distance in pixels between the medial edge of the eye and the front head, following a straight line, seen from the side; MN = distance in pixels between the caudal edge of the mouth and the nose, following a line perpendicular to the nose, seen from the side; A = angle between ME and MH; B = area in pixels of the head delimited by a square, seen from the side; EE = distance in pixels between the lateral edge of the ears, seen from above; EE2 = distance in pixels between the medial edge of the ears, seen from above; FH = larger diameter of the front head, seen from above; Bt = area in pixels of the front head delimited by a square, seen from above; CB = area in pixels of the front head delimited by a circle, seen from above; Le = length of the body in pixels, from the caudal edge of the head to the end of the body following the spine, seen from above.

phometric traits (e.g., $BrW_{CT} \sim BtW + EE$) were compared with an ANOVA. This statistical test was used to evaluate whether the inclusion of morphometric traits in addition to BtW results in a significant improvement in the models' ability to explain the variance in the dependent variables (BrW_{CT} , LW_{CT} , BrW_{CT}/LW_{CT}).

Results

The average BrW_{CT}/LW_{CT} determined in study 1 ($n = 310$) and study 2 ($n = 67$) was 0.62 ± 0.31 and 1.01 ± 0.42 [harmonic mean \pm SD], respectively (Table 1).

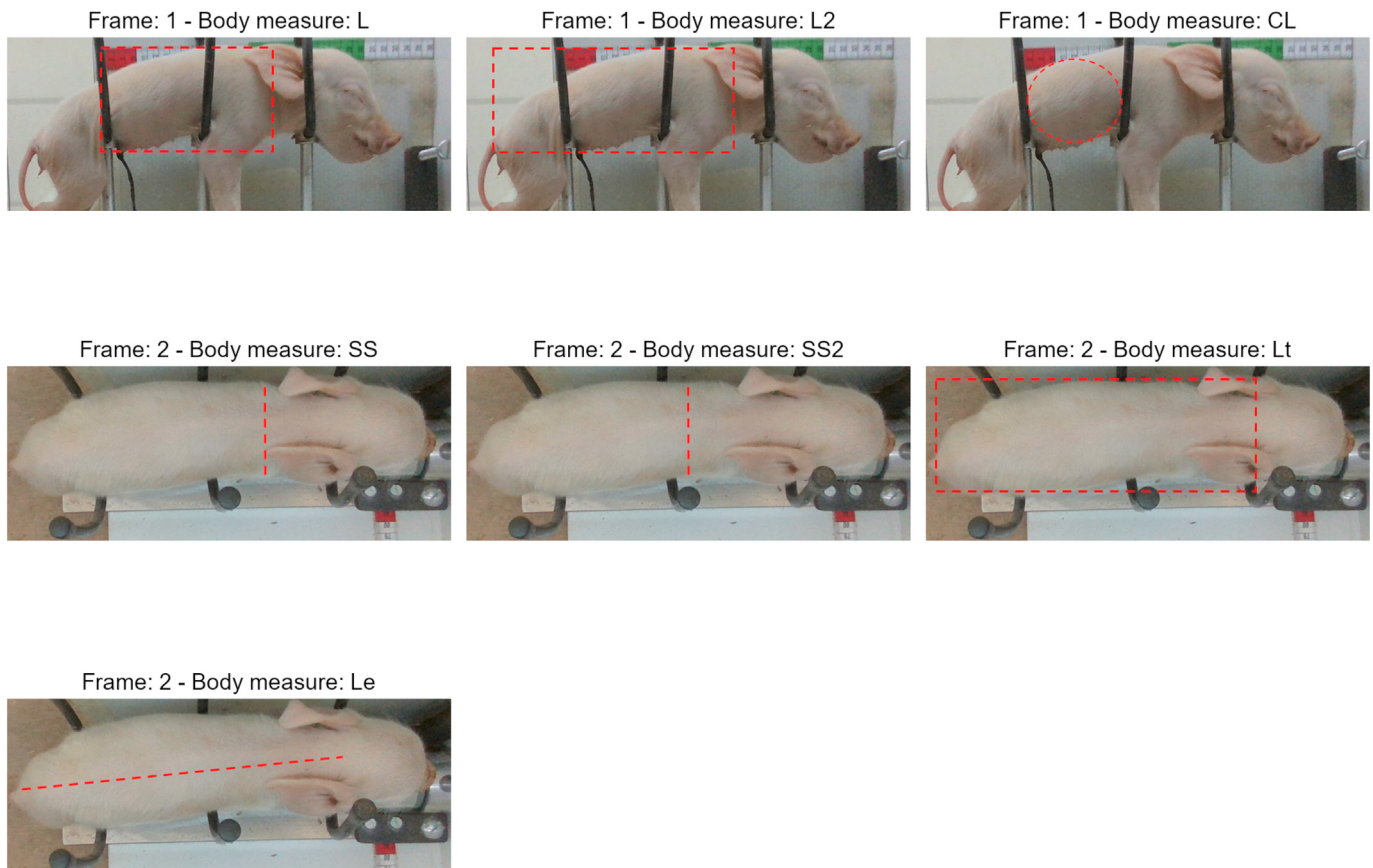


Fig. 3. Body measurements recorded to correlate with the weight of the liver of the piglets. Abbreviations: L = area in pixels of the body delimited by a square from the caudal edge of the head to the caudal edge of the abdomen, seen from the side; L2 = area in pixels of the body delimited by a square from the caudal edge of the head to the caudal edge of the body, seen from the side; CL = area in pixels of the abdomen delimited by a circle, seen from the side; SS = distance in pixels between the shoulders, seen from above; SS2 = diameter of the abdomen measured caudally to the shoulders, seen from above; Lt = area in pixels of the body delimited by a square from the caudal edge of the head to the caudal edge of the body, seen from above; Le = length of the body in pixels, from the caudal edge of the head to the end of the body following the spine, seen from above.

Brain weight, liver weight, and correlation between calculated computed tomography weight and actual weight of each organ

The euthanised piglets ($n = 30$) exhibited an average BrW_{Eu} of 32.3 ± 2.5 and BrW_{CT} of 34.4 ± 3.7 [mean \pm SD]. In terms of LW_{Eu} and LW_{CT} , the mean values were 58.1 ± 27.1 and 67.0 ± 33.5 , respectively. The average BrW_{Eu}/LW_{Eu} and BrW_{CT}/LW_{CT} were 0.57 ± 0.41 and 0.53 ± 0.41 [harmonic mean \pm SD], respectively (Table 1).

The correlation coefficients between the BrW , LW , and BrW/LW determined after death/euthanasia or by CT are presented in Table 2. Generally, the traits were highly correlated ($P < 0.001$), with values ranging from 0.83 for BrW to 0.97 for LW and BrW/LW . Based on these findings, we can confidently conclude that these measurements are sufficiently accurate for subsequent analysis.

Correlations between the body measurements taken on the images of the piglets by the authors and second observer

The subset of the morphometric traits ($n = 12$) measured on the selected piglets ($n = 144$, study one = 94, study two = 50) by the authors and the second observer were highly correlated ($P < 0.001$), with values ranging from 0.88 to 0.97 (see Supplementary Table S1).

Body measurements to predict brain weight, liver weight, and brain weight/liver weight ratio

Twenty morphometric measurements were taken from each pig ($n = 144$, study one = 94, study two = 50). The correlation coefficients between the BtW and each morphometric measurement with the BrW_{CT} or LW_{CT} are reported in Supplementary Table S2. The correlation coefficients ranged from -0.42 to 0.83 for the BrW_{CT} and from 0.80 to 0.88 for the LW_{CT} . Except for morphometric measurements A and EH, for which the correlation with the BrW_{CT} was not statistically significant, the other traits had r -values with P -values < 0.05 (Supplementary Table S2). The morphometric traits that were correlated with the BrW_{CT} ($n = 6$) and LW_{CT} ($n = 7$) with a $r \geq 0.70$ are reported in Table 3 and Table 4, respectively. These correlations are further illustrated in Fig. 4 and Fig. 5, respectively.

Using the morphometric measurements reported in Fig. 4 and Fig. 5, a variety of multiple linear regression models were computed to predict the BrW_{CT} (Table 5) and LW_{CT} (Table 6). The linear combination of the BtW and the distance between the lateral edge of the ears (EE, Fig. 2) showed the highest adjusted R^2 (adjusted $R^2 = 0.72$) in predicting the BrW_{CT} , followed by the distance between the medial edge of the ears (EE2, Fig. 2; adjusted $R^2 = 0.71$) and the area of the front head delimited by a square (Bt , Fig. 2; adjusted $R^2 = 0.71$) (Table 5). Regarding the LW_{CT} , the highest adjusted R^2 was achieved by the linear combination of BtW and the area of the body delimited by a square from the cau-

Table 1

Mean values of brain and liver weights and brain-to-liver weight ratio assessed in piglets after death/euthanasia (BrW_{Eu}, LW_{Eu}, BrW_{Eu}/LW_{Eu}), brain and liver weights and brain-to-liver weight ratio obtained from computed tomography (CT) scan volumes (BrW_{CT}, LW_{CT}, BrW_{CT}/LW_{CT}), and brain and liver weights and brain-to-liver weight ratio estimated from BrW_{Eu}, LW_{Eu}, BrW_{Eu}/LW_{Eu} through regression equations (estimated BrW_{CT}, estimated LW_{CT}, estimated BrW_{CT}/LW_{CT}).

Item	BrW			LW			BrW/LW		
	Mean ± SD			Mean ± SD			Harmonic mean ± SD		
	BrW _{Eu} ¹	BrW _{CT} ²	Estimated BrW _{CT} ³	LW _{Eu} ⁴	LW _{CT} ⁵	Estimated LW _{CT} ⁶	BrW _{Eu} /LW _{Eu} ⁷	BrW _{CT} /LW _{CT} ⁸	Estimated BrW _{CT} /LW _{CT} ⁹
Study 1									
All piglets (n = 310)	–	34.8 ± 3.1	–	–	57.0 ± 21.3	–	–	0.62 ± 0.31	–
Selected piglets (n = 94)	–	34.8 ± 2.8	–	–	57.3 ± 18.5	–	–	0.62 ± 0.3	–
Euthanised piglets (n = 30)	32.3 ± 2.5	34.4 ± 3.7	–	58.1 ± 27.1	67.0 ± 33.5	–	0.57 ± 0.41	0.53 ± 0.41	0.50 ± 0.40
Study 2									
All piglets (n = 67)	26.5 ± 3.2	–	27.4 ± 4.0	24.7 ± 9.7	–	27.1 ± 11.6	1.05 ± 0.44	–	1.01 ± 0.42
Selected piglets (n = 50)	27.0 ± 2.9	–	28.0 ± 3.6	25.1 ± 9.2	–	27.5 ± 11.0	1.10 ± 0.39	–	1.02 ± 0.38

Abbreviations: BrW = brain weight; LW = liver weight; BrW/LW = brain-to-liver weight ratio.

- ¹ BrW_{Eu} = brain weight assessed with a scale after euthanasia.
- ² BrW_{CT} = brain weight obtained from CT scan volume.
- ³ Estimated BrW_{CT} = estimated BrW_{CT} from the weight assessed after euthanasia (BrW_{Eu}) through the equation: $BrW_{CT} = (1.23 \times BrW_{Eu}) - 5.19$.
- ⁴ LW_{Eu} = liver weight assessed with a scale after euthanasia.
- ⁵ LW_{CT} = liver weight obtained from CT scan volume.
- ⁶ Estimated LW_{CT} = estimated LW_{CT} from the weight assessed after euthanasia (LW_{Eu}) through the equation: $LW_{CT} = (1.2 \times LW_{Eu}) - 2.57$.
- ⁷ BrW_{Eu}/LW_{Eu} = brain-to-liver weight ratio assessed with a scale after euthanasia.
- ⁸ BrW_{CT}/LW_{CT} = brain-to-liver weight ratio obtained from CT scan volumes.
- ⁹ Estimated BrW_{CT}/LW_{CT} = estimated BrW_{CT}/LW_{CT} from the brain-to-liver weight ratio assessed after euthanasia (BrW_{Eu}/LW_{Eu}) through the equation: $BrW_{CT}/LW_{CT} = (0.97 \times BrW_{Eu}/LW_{Eu}) - 0.014$.

Table 2

Simple linear regression models to correlate brain weight (BrW_{Eu}), liver weight (LW_{Eu}), and brain-to-liver weight ratio (BrW_{Eu}/LW_{Eu}) assessed after death/euthanasia of the piglets to brain weight (BrW_{CT}), liver weight (LW_{CT}), and brain-to-liver weight ratio (BrW_{CT}/LW_{CT}) obtained from computed tomography (CT) scan volumes.

Item	r	P-value ¹	R ² _{adj} ²	a ³	Intercept
BrW _{CT} ~BrW _{Eu} ⁴	0.83	< 0.001	0.68	1.23	-5.19
LW _{CT} ~LW _{Eu} ⁵	0.97	< 0.001	0.94	1.20	-2.57
BrW _{CT} /LW _{CT} ~BrW _{Eu} /LW _{Eu}	0.97	< 0.001	0.95	0.97	-0.01

Abbreviations: BrW = brain weight; LW = liver weight; BrW/LW = brain-to-liver weight ratio.

- ¹ P-value of r.
- ² R²_{adj} = adjusted R-squared.
- ³ a = slope of the regression line.
- ⁴ BrW_{Eu} = brain weight assessed with a scale on 30 piglets after euthanasia.
- ⁵ LW_{Eu} = liver weight assessed with a scale on 30 piglets after euthanasia.

Table 3

Correlation coefficients between birth body weight (BtW)/morphometric measurements and brain weight (BrW_{CT}) determined after computed tomography scan or death/euthanasia of the piglets.

Item	Mean	SD	r	P-value ¹
BtW, kg	1.21	0.41	0.83	< 0.001
EE, pixel	203.0	47.3	0.82	< 0.001
Bt, pixel ²	29 567.3	8 684.5	0.78	< 0.001
EE2, pixel	122.8	28.4	0.77	< 0.001
Le, pixel	679.4	116.7	0.75	< 0.001
FH, pixel	173.8	30.3	0.75	< 0.001
CB, pixel ²	22 812.9	6 874.8	0.74	< 0.001

Abbreviations: BtW = birth body weight in kg; EE = distance in pixels between the lateral edge of the ears, seen from above; Bt = area in pixels of the front head delimited by a square, seen from above; EE2 = distance in pixels between the medial edge of the ears, seen from above; Le = length of the body in pixels, from the caudal edge of the head to the end of the body following the spine, seen from above; FH = larger diameter in pixels of the front head, seen from above; CB = area in pixels of the front head delimited by a circle, seen from above.

- ¹ P-value of r.

dal edge of the head to the caudal edge of the body (Lt, Fig. 3; adjusted R² = 0.80), followed by the area of the body delimited by a square from the caudal edge of the head to the caudal edge of the abdomen (L, Fig. 3; adjusted R² = 0.79) and the length of the body, from the caudal edge of the head to the end of the body following the spine (Le, Fig. 3; adjusted R² = 0.79) (Table 6).

The six morphometric measurements (EE, EE2, and Bt to estimate the BrW_{CT} and Lt, L, and Le to estimate the LW_{CT}) which, in combination with the BtW, showed the highest adjusted R² in the multiple linear regressions were selected and used to develop equations in the training dataset to calculate the BrW_{CT} and LW_{CT}. The degree of correlation between the true and the predicted

Table 4

Correlation coefficients between birth body weight (BtW)/morphometric measurements and liver weight (LW_{CT}) determined after computed tomography scan or death/euthanasia of the piglets.

Item	Mean	SD	r	P-value ¹
BtW, kg	1.21	0.41	0.88	< 0.001
Lt, pixel ²	170 214	59 375	0.87	< 0.001
L2, pixel ²	103 262	34 286	0.86	< 0.001
L, pixel ²	69 156	19 645	0.86	< 0.001
SS2, pixel	209.7	42.5	0.84	< 0.001
SS, pixel	220.1	42.8	0.83	< 0.001
CL, pixel ²	25 761	8 916	0.83	< 0.001
Le, pixel	679.4	116.7	0.80	< 0.001

Abbreviations: BtW = birth body weight in kg; Lt = area in pixels of the body delimited by a square from the caudal edge of the head to the caudal edge of the body, seen from above; L2 = area in pixels of the body delimited by a square from the caudal edge of the head to the caudal edge of the body, seen from the side; L = area in pixels of the body delimited by a square, from the caudal edge of the head to the caudal edge of the abdomen, seen from the side; SS2 = diameter in pixels of the abdomen measured caudally of the shoulders, seen from above; SS = distance in pixels between the shoulders, seen from above; CL = area in pixels of the abdomen delimited by a circle, seen from the side; Le = length of the body in pixels, from the caudal edge of the head to the end of the body following the spine, seen from above.

¹ P-value of r.

BrW_{CT} and LW_{CT} was tested in the training and testing datasets and is reported in Fig. 6 and Fig. 7, respectively.

The three regression equations (Table 7), developed to predict the BrW_{CT}, showed similar performance. When EE was used alongside BtW (BrW_{CT}~BtW+EE), the resulting MAE and MAPE between true and predicted BrW_{CT} values were 1.78 and 0.06 in the training dataset (Table 8) and 1.95 and 0.06 in the testing dataset, respectively (Table 9). The correlation coefficient between true and predicted BrW_{CT} values was 0.85 and 0.84 in the training (Table 8) and testing dataset (Table 9), respectively. When EE2 was included in combination with the BtW (BrW_{CT}~BtW+EE2), the MAE and MAPE between the true and the predicted BrW_{CT} values were 1.74 and 0.06 in the training dataset (Table 8) and 2.07 and 0.07 in the testing dataset (Table 9), respectively. The correlation coefficient between true and predicted BrW_{CT} values was 0.85 and 0.82 in the training (Table 8) and testing dataset (Table 9), respectively. Similarly, when Bt was included in combination with the BtW (BrW_{CT}~BtW+Bt), the MAE and MAPE between the true and the predicted BrW_{CT} values were 1.79 and 0.06 in the training dataset (Table 8) and 1.99 and 0.06 in the testing dataset (Table 9), respectively. The correlation coefficient between true and predicted BrW_{CT} values was 0.84 and 0.83 in the training (Table 8) and testing dataset (Table 9), respectively.

Of the three regression equations (Table 7) predicting the LW_{CT}, the one which showed better performance included the combination of BtW and L (LW_{CT}~BtW+L). In this case, the MAE and MAPE were equal to 7.03 and 0.16 in the training dataset (Table 8) and 9.29 and 0.17 in the testing dataset (Table 9), respectively. The correlation coefficient between true and predicted LW_{CT} values was 0.89 and 0.90 in the training (Table 8) and testing dataset (Table 9), respectively.

As previously described, two approaches were tested to predict the BrW_{CT}/LW_{CT}. In the first approach, an equation was constructed on the training dataset to estimate the BrW_{CT}/LW_{CT} by incorporating the measures EE (Fig. 2) and L (Fig. 3), along with the BtW (BrW_{CT}/LW_{CT}~BtW+EE+L). The BtW, EE and L were the measures that better predicted the BrW_{CT} and LW_{CT}. In the second approach, the values of BrW_{CT} and LW_{CT} estimated with EE in combination with BtW (BrW_{CT}~BtW+EE) and L in combination with BtW (LW_{CT}~BtW+L), respectively, were directly employed to determine the BrW_{CT}/LW_{CT}. The degree of correlation between the true and the predicted BrW_{CT}/LW_{CT} was tested in the training and testing datasets for the first (Fig. 8 and Fig. 9, panel A) and the second approach (Fig. 8 and Fig. 9, panel C). Using the first approach, the MAE and MAPE between the true and predicted BrW_{CT}/LW_{CT} were equal to 0.16 and 0.19 in the training dataset (Table 8) and 0.14 and 0.17 in the testing dataset, respectively (Table 9). The correlation coef-

ficient between true and predicted BrW_{CT}/LW_{CT} was 0.80 and 0.85 in the training (Table 8) and testing dataset (Table 9), respectively.

For the second approach, the MAE and MAPE between the true and predicted BrW_{CT}/LW_{CT} were equal to 0.16 and 0.19 in the training (Table 8) and to 0.14 and 0.20 in the testing dataset, respectively (Table 9). The correlation coefficient between true and predicted BrW_{CT}/LW_{CT} was 0.81 and 0.88 in the training (Table 8) and testing dataset (Table 9), respectively.

When BtW was used alone to predict BrW_{CT} (BrW_{CT}~BtW), the resulting MAE and MAPE between the true and the predicted BrW_{CT} values were similar to those of the models including the various morphometric traits (BrW_{CT}~BtW+EE; BrW_{CT}~BtW+EE2; BrW_{CT}~BtW+Bt), showing values of 1.80 and 0.06 in the training dataset (Table 8) and 2.17 and 0.07 in the testing dataset, respectively (Table 9). The correlation coefficient between true and predicted BrW_{CT} values was 0.84 and 0.80 in the training (Table 8) and testing dataset (Table 9), respectively. In line with the trend observed for BrW_{CT}, when BtW was used as the only independent variable to predict the LW_{CT} (LW_{CT}~BtW), the resulting MAE and MAPE values were similar to those obtained with the models including the various morphometric traits (LW_{CT}~BtW+L; LW_{CT}~BtW+Lt; BrW_{CT}~BtW+Le), showing values of 6.95 and 0.18 in the training dataset (Table 8) and 8.73 and 0.18 in the testing dataset, respectively (Table 9). The correlation coefficient between true and predicted LW_{CT} values was 0.89 and 0.89 in the training (Table 8) and testing dataset (Table 9), respectively. The BrW_{CT}/LW_{CT} was also estimated using the BtW alone, according to the first (Supplementary Fig. S1 and S2, panel A) and second approach (Supplementary Fig. S3 and S4, panel A). In the first case, the MAE and MAPE between the true and predicted BrW_{CT}/LW_{CT} were equal to 0.17 and 0.19 in the training dataset (Table 8) and 0.15 and 0.18 in the testing dataset (Table 9), respectively. The correlation coefficient between true and predicted BrW_{CT}/LW_{CT} was 0.77 and 0.83 in the training (Table 8) and testing dataset (Table 9), respectively. For the second approach, the MAE and MAPE between the true and predicted BrW_{CT}/LW_{CT} were equal to 0.16 and 0.18 in the training (Table 8) and to 0.14 and 0.18 in the testing dataset (Table 9), respectively. The correlation coefficient between true and predicted BrW_{CT}/LW_{CT} was 0.79 and 0.87 in the training (Table 8) and testing dataset (Table 9), respectively.

The error rates in predicting BrW_{CT}, LW_{CT}, and BrW_{CT}/LW_{CT} were similar, or in some cases even lower when using BtW as the sole independent variable or in conjunction with morphometric traits. However, the correlation coefficients between the true and predicted BrW_{CT}, LW_{CT}, and BrW_{CT}/LW_{CT} values in the testing dataset were always higher when using the BtW in combination

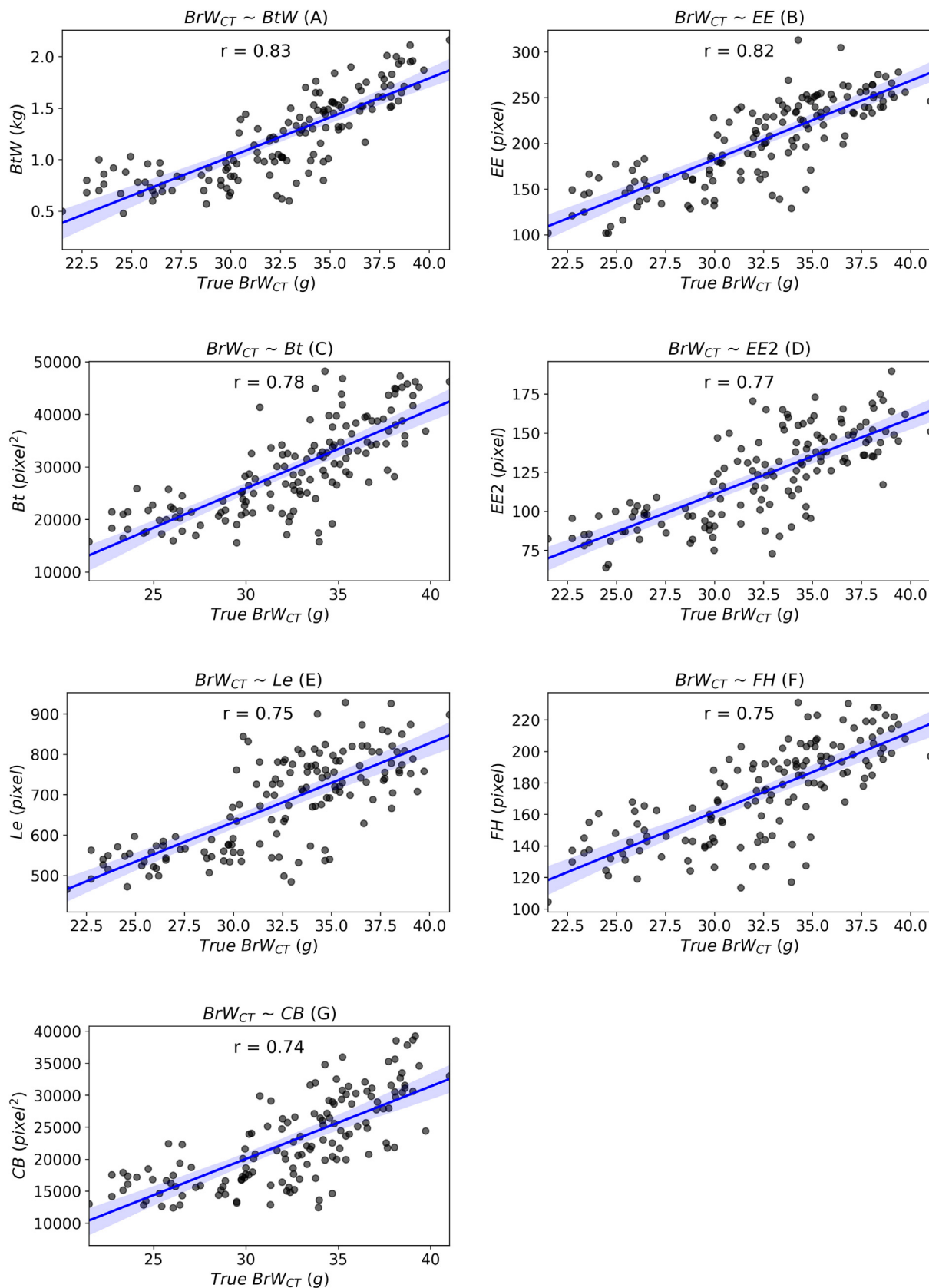


Fig. 4. Variables which showed a $r \geq 0.70$ in the linear correlation with brain weight (BrW_{CT}) of the piglets. X-Axis: BrW_{CT} (g); y-axis: (A) birth body weight (BtW) expressed in kg; (B) EE = distance in pixels between the lateral edge of the ears, seen from above; (C) Bt = area in pixels of the front head delimited by a square, seen from above; (D) EE2 = distance in pixels between the medial edge of the ears, seen from above; (E) Le = length of the body in pixels, from the caudal edge of the head to the end of the body following the spine, seen from above; (F) FH = larger diameter of the front head, seen from above; (G) CB = area in pixels of the front head delimited by a circle, seen from above.

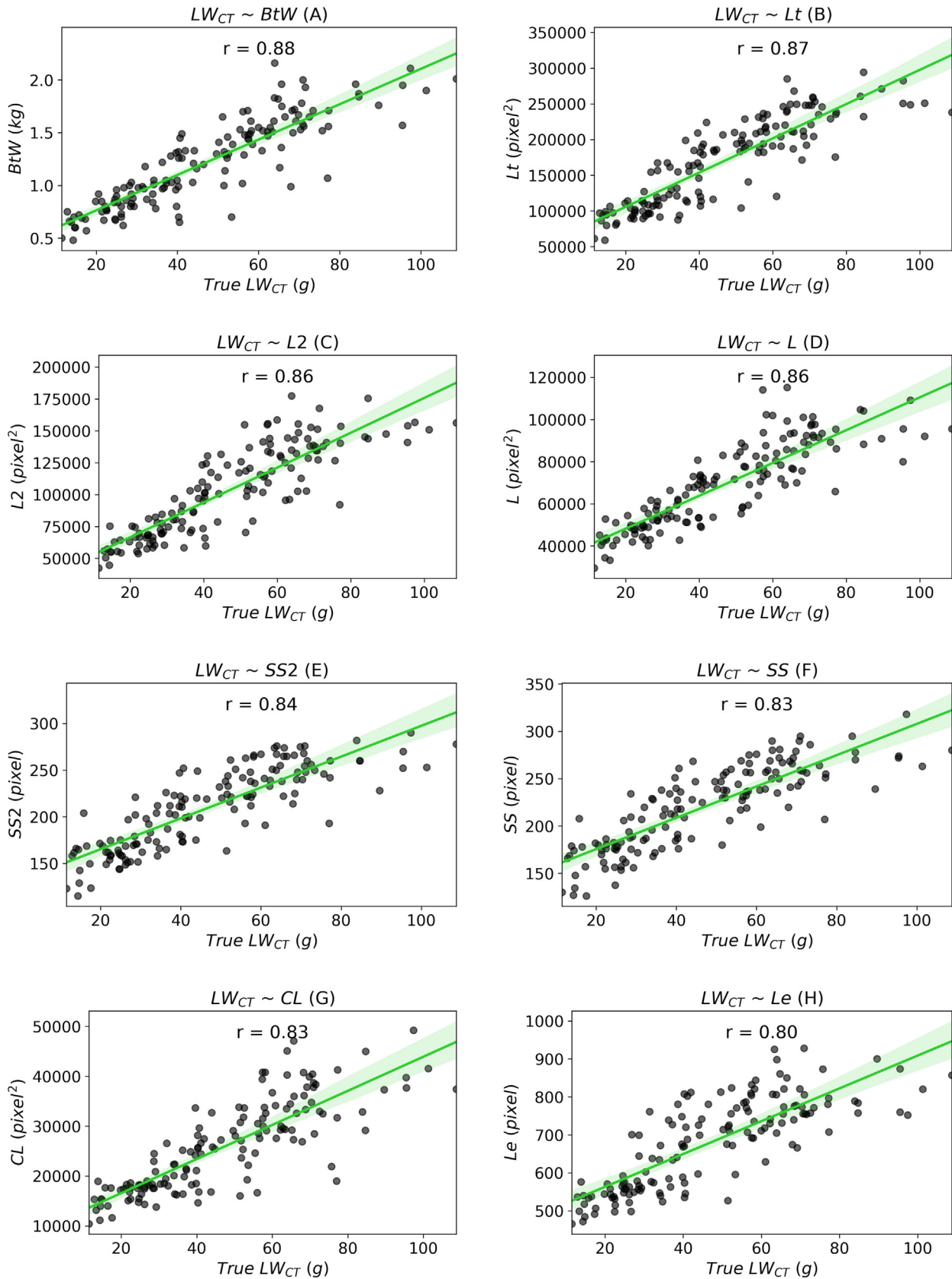


Fig. 5. Variables which showed a $r \geq 0.70$ in the linear correlation with the liver weight (LW_{CT}) of the piglets. X-Axis: LW_{CT} (g); y-axis: (A) birth body weight (BtW) expressed in kg; (B) Lt = area in pixels of the body delimited by a square from the caudal edge of the head to the caudal edge of the body, seen from above; (C) L2 = area in pixels of the body delimited by a square from the caudal edge of the head to the caudal edge of the body, seen from the side; (D) L = area in pixels of the body delimited by a square from the caudal edge of the head to the caudal edge of the abdomen, seen from the side; (E) SS2 = diameter of the abdomen measured caudally of the shoulders, seen from above; (F) SS = distance in pixels between the shoulders, seen from above; (G) CL = area in pixels of the abdomen delimited by a circle, seen from the side; (H) Le = length of the body in pixels, from the caudal edge of the head to the end of the body following the spine, seen from above.

Table 5

Adjusted R^2 values (R^2_{adj}) of multiple linear regression models to predicted brain weight (BrW_{CT}) determined after computed tomography (CT) scan or death/euthanasia of the piglets from birth weight (BtW) and morphometric measurements.

Item	R^2_{adj} ¹	a1 ²	a2 ³	Intercept
$BrW_{CT} \sim BtW + EE$	0.72	5.39	0.04	18.4
$BrW_{CT} \sim BtW + EE2$	0.71	6.76	0.04	19.1
$BrW_{CT} \sim BtW + Bt$	0.71	6.75	0.0001	20.3
$BrW_{CT} \sim BtW + CB$	0.70	7.31	0.0001	20.5
$BrW_{CT} \sim BtW + Le$	0.70	7.37	0.007	18.5
$BrW_{CT} \sim BtW + FH$	0.70	7.43	0.03	18.7
$BrW_{CT} \sim BtW$	0.69	9.12	–	21.4

Abbreviations: BrW = brain weight; BtW = birth body weight; EE = distance between the lateral edge of the ears, seen from above; EE2 = distance between the medial edge of the ears, seen from above; Bt = area of the front head delimited by a square, seen from above; CB = area of the front head delimited by a circle, seen from above; Le = length of the body, from the caudal edge of the head to the end of the body following the spine, seen from above; FH = larger diameter of the front head, seen from above.

¹ R^2_{adj} = adjusted R-square.

² a1 = regression coefficient associated with the first predictor variable (BtW).

³ a2 = regression coefficient associated with the second predictor variable (EE; EE2; Bt; CB; Le; FH).

Table 6

Adjusted R^2 values (R^2_{adj}) of multiple linear regression models to predicted the liver weight (LW_{CT}) determined after computed tomography (CT) scan or death/euthanasia of the piglets from birth weight (BtW) and morphometric measurements.

Item	R^2_{adj} ¹	a1 ²	a2 ³	Intercept
$LW_{CT} \sim BtW + Lt$	0.80	27.3	0.0001	–10.8
$LW_{CT} \sim BtW + L$	0.79	33.0	0.0003	–14.2
$LW_{CT} \sim BtW + Le$	0.79	37.5	0.04	–24.2
$LW_{CT} \sim BtW + L2$	0.78	33.9	0.0002	–10.7
$LW_{CT} \sim BtW + SS2$	0.78	36.3	0.11	–19.8
$LW_{CT} \sim BtW + SS$	0.78	37.5	0.1	–19.5
$LW_{CT} \sim BtW + CL$	0.78	40.9	0.0003	–9.95
$LW_{CT} \sim BtW$	0.78	46.5	–	–9.53

Abbreviations: LW = liver weight; BtW = birth body weight; Lt = area of the body delimited by a square from the caudal edge of the head to the caudal edge of the body, seen from above; L = area of the body delimited by a square from the caudal edge of the head to the caudal edge of the abdomen, seen from the side; Le = length of the body, from the caudal edge of the head to the end of the body following the spine, seen from above; L2 = area of the body delimited by a square from the caudal edge of the head to the caudal edge of the body, seen from the side; SS2 = diameter of the abdomen measured caudally to the shoulders, seen from above; SS = distance between the shoulders, seen from above; CL = area of the abdomen delimited by a circle, seen from the side.

¹ R^2_{adj} = adjusted R-square.

² a1 = regression coefficient associated with the first predictor variable (BtW).

³ a2 = regression coefficient associated with the second predictor variable (Lt; L; Le; L2; SS2; SS; CL).

with the morphometric traits compared to BtW alone, with the only exception of Le. Using the BtW alone ($LW_{CT} \sim BtW$) or in combination with Le ($LW_{CT} \sim BtW + Le$) resulted in the same correlation coefficient between true and estimated LW_{CT} in the testing dataset. Moreover, comparisons conducted through ANOVA between models that exclusively involve BtW (e.g., $BrW_{CT} \sim BtW$) and those that incorporate BtW alongside morphometric traits (e.g., $BrW_{CT} \sim BtW + EE$) illustrate a significant enhancement in model fit with the addition of each morphometric trait ($P < 0.05$). These results imply that incorporating morphometric traits along with BtW in the models increases their ability to predict the variable of interest (BrW_{CT} , LW_{CT} , BrW_{CT}/LW_{CT}). The sole exception was observed with the variable Bt. The lack of significance in the coefficient for Bt in the model ($BrW_{CT} \sim BtW + Bt$) and the non-significant results from the ANOVA indicate that this particular variable might not hold relevance or contribute significantly to explaining the variability in BrW_{CT} when BtW is already incorporated into the model.

Body measurements to predict the brain-to-liver weight ratio in piglets with a birth weight above 800 g

When the equation to predict the BrW_{CT}/LW_{CT} developed in the first approach ($BrW_{CT}/LW_{CT} \sim BtW + EE + L$) was tested on piglets with a BtW > 800 g, the performance did not change considerably. For the first approach, the MAE and MAPE between the true and predicted BrW_{CT}/LW_{CT} were equal to 0.12 and 0.16 in the training

(Table 8) and to 0.11 and 0.18 in the testing dataset, respectively (Table 9). When the estimated BrW_{CT} ($BrW_{CT} \sim BtW + EE$) and LW_{CT} ($LW_{CT} \sim BtW + L$) were used to predict the BrW_{CT}/LW_{CT} in piglets with a BtW > 800 g, according to the second approach, the MAE and MAPE between the true and predicted BrW_{CT}/LW_{CT} were equal to 0.12 and 0.16 in the training dataset (Table 8) and 0.12 and 0.21 in the testing dataset (Table 9). The degree of correlation between the true and the predicted BrW_{CT}/LW_{CT} was tested in the training and testing datasets for the first (Fig. 8 and Fig. 9, panel B) and the second approach (Fig. 8 and Fig. 9, panel D).

The correlation coefficient between true and predicted BrW_{CT}/LW_{CT} values according to the first approach was 0.78 and 0.79 in the training (Table 8) and testing dataset (Table 9), respectively. The correlation coefficient between true and predicted BrW_{CT}/LW_{CT} values according to the second approach was 0.81 and 0.75 in the training (Table 8) and testing dataset (Table 9), respectively.

The performance of the models including BtW as the sole predictor was also tested on piglets with a BtW > 800 g according to the first (Supplementary Fig. S1 and S2, panel B) and the second approach (Supplementary Fig. S3 and S4, panel B). When the equation to predict the BrW_{CT}/LW_{CT} developed in the first approach ($BrW_{CT}/LW_{CT} \sim BtW$) was tested on piglets with a BtW > 800 g MAE and MAPE between the true and predicted BrW_{CT}/LW_{CT} were equal to 0.12 and 0.17 in the training (Table 8) and to 0.11 and 0.19 in the testing dataset (Table 9), respectively. The correlation coefficient between true and predicted BrW_{CT}/LW_{CT} values was 0.77

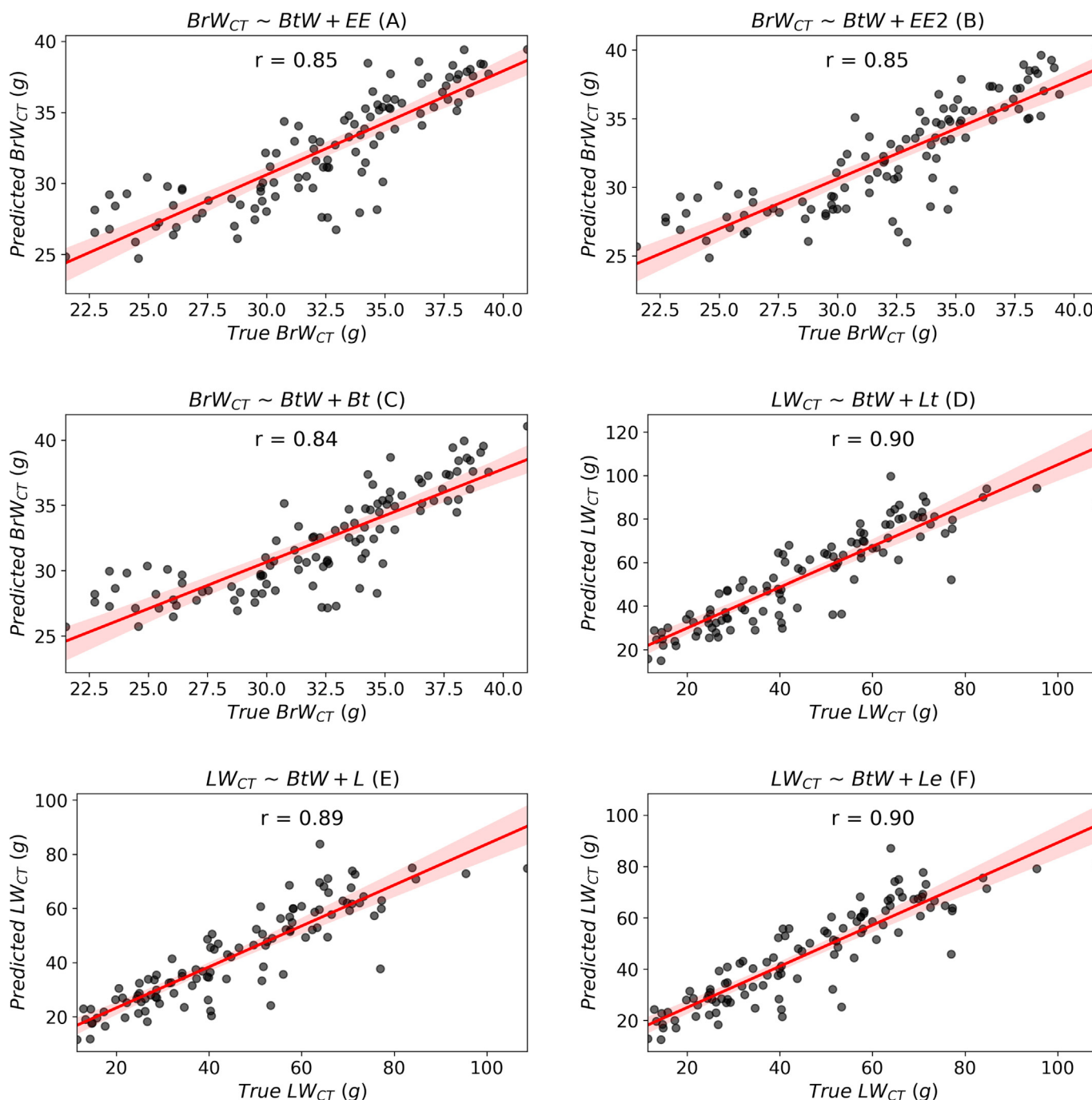


Fig. 6. Linear regressions between true and predicted BrW_{CT} and LW_{CT} of the piglets of the training dataset. X-Axis: true brain weight (true BrW_{CT}) (panels A, B, C) and true liver weight (true LW_{CT}) (panels D, E, F); y-axis: (A) brain weight (predicted BrW_{CT}) between the lateral edge of the ears, seen from above (EE); (B) brain weight (predicted BrW_{CT}) predicted from BtW expressed in kg, and the distance in pixels between the medial edge of the ears, seen from above (EE2); (C) brain weight (predicted BrW_{CT}) predicted from BtW expressed in kg, and the area in pixels of the front head delimited by a square, seen from above (Bt); (D) liver weight (predicted LW_{CT}) predicted from BtW and the area in pixels of the body delimited by a square from the caudal edge of the head to the caudal edge of the body, seen from above (Lt); (E) liver weight (predicted LW_{CT}) predicted from BtW expressed in kg, and the area in pixels of the body delimited by a square from the caudal edge of the head to the caudal edge of the abdomen, seen from the side (L); (F) liver weight (predicted LW_{CT}) predicted from BtW expressed in kg, and the length of the body in pixels, from the caudal edge of the head to the end of the body following the spine; seen from above (Le).

and 0.72 in the training (Table 8) and testing dataset (Table 9), respectively.

When the estimated BrW_{CT} ($BrW_{CT} \sim BtW$) and LW_{CT} ($LW_{CT} \sim BtW$) were used to predict the BrW_{CT}/LW_{CT} in piglets with a

$BtW > 800$ g, according to the second approach, the MAE and MAPE between the true and predicted BrW_{CT}/LW_{CT} were equal to 0.12 and 0.15 in the training dataset (Table 8) and 0.11 and 0.18 in the testing dataset (Table 9), respectively. The correlation coeffi-

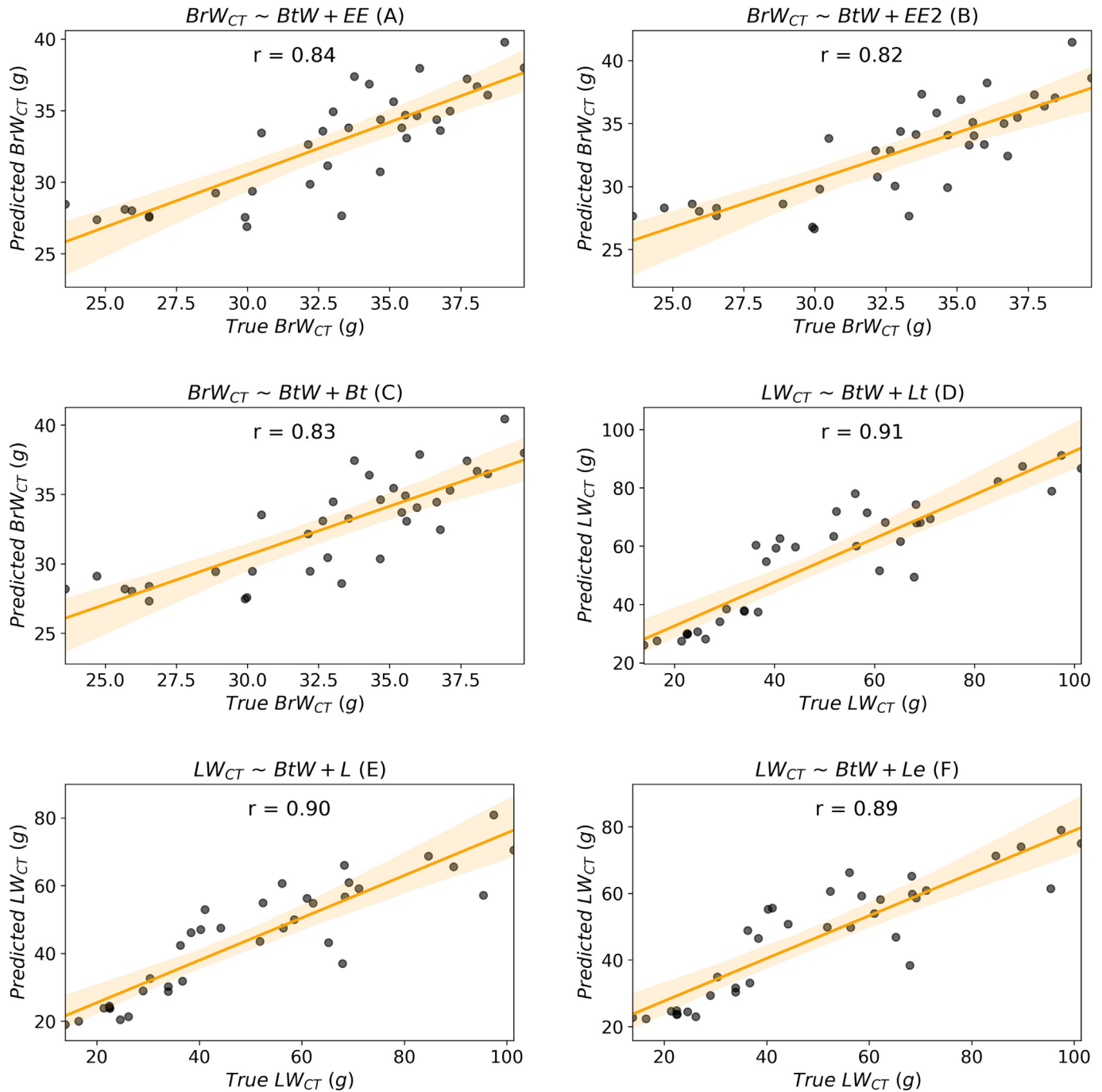


Fig. 7. Linear regressions between true and predicted BrW_{CT} and LW_{CT} of the piglets of the testing dataset. X-Axis: true brain weight (true BrW_{CT}) (panels A, B, C) and true liver weight (true LW_{CT}) (panels D, E, F); y-axis: (A) brain weight (predicted BrW_{CT}) predicted from the birth body weight (BtW) expressed in kg, and the distance in pixels between the lateral edge of the ears, seen from above (EE); (B) brain weight (predicted BrW_{CT}) predicted from BtW expressed in kg, and the distance in pixels between the medial edge of the ears, seen from above ($EE2$); (C) brain weight (predicted BrW_{CT}) predicted from BtW expressed in kg, and the area in pixels of the front head delimited by a square, seen from above (Bt); (D) liver weight (predicted LW_{CT}) predicted from BtW expressed in kg, and the area in pixels of the body delimited by a square from the caudal edge of the head to the caudal edge of the body, seen from above (Lt); (E) liver weight (predicted LW_{CT}) predicted from BtW expressed in kg, and the area in pixels of the body delimited by a square from the caudal edge of the head to the caudal edge of the abdomen, seen from the side (L); (F) liver weight (predicted LW_{CT}) predicted from BtW expressed in kg, and the length of the body in pixels, from the caudal edge of the head to the end of the body following the spine, seen from above (Le).

Table 7

Regression equations developed with the training dataset to predict brain weight (BrW_{CT}), liver weight (LW_{CT}), and brain-to-liver weight ratio (BrW_{CT}/LW_{CT}) determined by computed tomography (CT) or death/euthanasia of the piglets.

Item	Equation
BrW _{CT}	
BrW _{CT} ~BtW+EE	$BrW_{CT} = 18.6 + 6.06 \times BtW + 0.03 \times EE$
BrW _{CT} ~BtW+Bt	$BrW_{CT} = 20.5 + 7.56 \times BtW + 9.183e^{-05} \times Bt$
BrW _{CT} ~BtW+EE2	$BrW_{CT} = 18.8 + 7.02 \times BtW + 0.04 \times EE2$
BrW _{CT} ~BtW	$BrW_{CT} = 21.1 + 9.28 \times BtW$
LW _{CT}	
LW _{CT} ~BtW+Lt	$LW_{CT} = -8.13 + 23.5 \times BtW + 0.0002 \times Lt$
LW _{CT} ~BtW+L	$LW_{CT} = -10.9 + 33.2 \times BtW + 0.0002 \times L$
LW _{CT} ~BtW+Le	$LW_{CT} = -24.4 + 33.1 \times BtW + 0.04 \times Le$
LW _{CT} ~BtW	$LW_{CT} = -7.19 + 44.0 \times BtW$
BrW _{CT} /LW _{CT}	
BrW _{CT} /LW _{CT} ~BtW+EE+L ¹	$\log(BrW_{CT}/LW_{CT}) = 0.839 + -0.377 \times BtW + -0.0007 \times EE + -7.165e^{-06} \times L$
BrW _{CT} ~BtW+EE / LW _{CT} ~BtW+L ²	$BrW_{CT}/LW_{CT} = \frac{BrW_{CT}=18.4+5.39 \times BtW+0.04 \times EE}{LW_{CT}=-14.2+33 \times BtW+0.0003 \times L}$
BrW _{CT} /LW _{CT} ~BtW ³	$\log(BrW_{CT}/LW_{CT}) = 0.677 + -0.765 \times BtW$
BrW _{CT} ~BtW / LW _{CT} ~BtW ⁴	$BrW_{CT}/LW_{CT} = \frac{BrW_{CT}=21.1+9.28 \times BtW}{LW_{CT}=-7.19+44.0 \times BtW}$

Abbreviations: BrW = brain weight; LW = liver weight; BtW = birth body weight in kg; EE = distance in pixels between the lateral edge of the ears, seen from above; Bt = area in pixels of the front head delimited by a square, seen from above; EE2 = distance in pixels between the medial edge of the ears, seen from above; Lt = area of the body in pixels delimited by a square from the caudal edge of the head to the caudal edge of the body, seen from above; L = area of the body in pixels delimited by a square from the caudal edge of the head to the caudal edge of the abdomen, seen from the side; Le = length of the body in pixels, from the caudal edge of the head to the end of the body following the spine, seen from above.

¹ BrW_{CT}/LW_{CT}~BtW+EE+L = brain-to-liver weight ratio predicted according to the first approach. An equation was constructed on the training dataset to estimate the BrW_{CT}/LW_{CT} by incorporating the distance between the lateral edges of the ears (EE) and the area of the body delimited by a square from the caudal edge of the head to the caudal edge of the abdomen (L), along with the BtW. These were the measures that better predicted the BrW_{CT} and LW_{CT}.

² BrW_{CT}~BtW+EE / LW_{CT}~BtW+L = brain-to-liver weight ratio predicted according to the second approach. The values of BrW_{CT} and LW_{CT} estimated with the equations developed in the training dataset, derived from EE in combination with BtW and L in combination with BtW, respectively, were directly employed to determine the BrW_{CT}/LW_{CT}.

³ BrW_{CT}/LW_{CT}~BtW = brain-to-liver weight ratio predicted according to the first approach but using the BtW as sole predictor. An equation was constructed on the training dataset to estimate the BrW_{CT}/LW_{CT} by incorporating only the BtW as independent variable.

⁴ BrW_{CT}~BtW / LW_{CT}~BtW = brain-to-liver weight ratio predicted according to the second approach but using the BtW as sole predictor. The values of BrW_{CT} and LW_{CT} estimated with the equations developed in the training dataset incorporating only the BtW as independent variable, were directly employed to determine the BrW_{CT}/LW_{CT}.

cient between true and predicted BrW_{CT}/LW_{CT} values was 0.79 and 0.69 in the training (Table 8) and testing dataset (Table 9), respectively.

Discussion

Brain weight, liver weight, and correlation between calculated computed tomography weight and actual weight of each organ

In this study, 30 piglets were euthanized to measure the weight of the brain and the liver using two methods: directly with a scale after euthanasia (BrW_{Eu}, LW_{Eu}, and BrW_{Eu}/LW_{Eu}) and by calculating the volumes from CT scan images and multiplying these volumes by the organ densities (BrW_{CT}, LW_{CT}, and BrW_{CT}/LW_{CT}). The data obtained were used to develop regression equations for converting post-euthanasia weights into weights derived from CT scan volumes. The results showed a near-perfect correlation between the liver weights measured post-euthanasia and those extrapolated from CT scan volumes, as well as for the BrW/LW. However, the correlation between the brain weights measured post-euthanasia and those extrapolated from CT volumes was slightly lower, indicating that the two methodologies did not align as well for the brain as they did for the liver and the organs' ratio. Unfortunately, we could not determine the exact cause of the discrepancy between the actual brain weight and the brain weight extrapolated from CT scan volumes. The brain might undergo different post-mortem changes compared to the liver, such as fluid loss or swelling, affecting weight measurements. In addition, while average brain density was calculated based on 30 piglets, individual variations in brain tissue density might still affect the accuracy of volume-to-weight conversions. Despite these factors, the corre-

lation coefficient for brain weight remained highly significant, indicating a strong relationship between CT-derived brain weights and those measured post-euthanasia. Given that only 50 out of the 144 piglets selected for analysis had actual brain weights available, we decided to convert all post-euthanasia weights to CT-derived weights for consistency. This approach ensures a uniform data set for analysis. However, the noted discrepancy in brain weights necessitates further investigation to understand the underlying causes and implications. Future studies should aim to explore these aspects to minimize potential biases in these conversions.

Body measurements to predict brain weight, liver weight, and brain weight/liver weight ratio

Foetal growth restriction often occurs as a result of chronic placental insufficiency, which hampers the delivery of sufficient oxygen and nutrients to the foetus in the uterus, leading to abnormal foetal development (Chand et al., 2022; Cohen et al., 2015). As a consequence, IUGR piglets can be identified by their distinctive head shape and low BtW. However, in a previous study (Ruggeri et al., 2024), we demonstrated that identification of IUGR piglets solely based on head morphology or BtW does not always agree with an increased BrW/LW and can lead to inaccurate classification of this condition. For these reasons, to accurately assess growth restriction in piglets, measurements such as BtW and head shape should be complemented by evaluating the relative brain-to-body weight or BrW/LW ratio, as these directly reflect the brain-sparing effect (Chand et al., 2022; Felicioni et al., 2019).

In this study, the BtW, together with the weights of the brain and liver of newborn piglets were measured, and pictures of the same piglets were taken to capture specific body measure-

Table 8

r, P-value of r, mean absolute error (MAE), mean absolute percentage error (MAPE), RMSE, RMSE % and coefficient of correlation and concordance (CCC) between true and predicted brain weight (BrW_{CT}), liver weight (LW_{CT}), and brain-to-liver weight ratio (BrW_{CT}/LW_{CT}) of the piglets in the training dataset.

Item	r	P-value ¹	MAE	MAPE	RMSE	RMSE %	CCC
BrW _{CT}							
BrW _{CT} ~BtW+EE	0.85	< 0.001	1.78	0.06	2.37	7.36	0.84
BrW _{CT} ~BtW+Bt	0.84	< 0.001	1.79	0.06	2.45	7.59	0.83
BrW _{CT} ~BtW+EE2	0.85	< 0.001	1.74	0.06	2.38	7.38	0.84
BrW _{CT} ~BtW	0.84	< 0.001	1.80	0.06	2.48	7.69	0.83
LW _{CT}							
LW _{CT} ~BtW+Lt	0.90	< 0.001	10.7	0.28	12.6	27.5	0.90
LW _{CT} ~BtW+L	0.89	< 0.001	7.03	0.16	9.90	21.7	0.88
LW _{CT} ~BtW+Le	0.90	< 0.001	6.75	0.17	9.13	19.9	0.89
LW _{CT} ~BtW	0.89	< 0.001	6.95	0.18	9.57	20.9	0.88
BrW _{CT} /LW _{CT}							
BrW _{CT} /LW _{CT} ~BtW+EE+L ²	0.80	< 0.001	0.16	0.19	0.24	28.1	0.73
BrW _{CT} /LW _{CT} ~BtW+EE+L (BtW>800 g) ³	0.78	< 0.001	0.12	0.16	0.16	19.7	0.76
BrW _{CT} ~BtW+EE / LW _{CT} ~BtW+L ⁴	0.81	< 0.001	0.16	0.19	0.23	28.0	0.79
BrW _{CT} ~BtW+EE / LW _{CT} ~BtW+L (BtW>800 g) ⁵	0.81	< 0.001	0.12	0.16	0.15	19.0	0.76
BrW _{CT} /LW _{CT} ~BtW ⁶	0.77	< 0.001	0.17	0.19	0.25	29.3	0.71
BrW _{CT} /LW _{CT} ~BtW (BtW>800 g) ⁷	0.77	< 0.001	0.12	0.17	0.16	20.1	0.75
BrW _{CT} ~BtW / LW _{CT} ~BtW ⁸	0.79	< 0.001	0.16	0.18	0.24	28.4	0.75
BrW _{CT} ~BtW / LW _{CT} ~BtW (BtW>800 g) ⁹	0.79	< 0.001	0.12	0.15	0.17	19.8	0.71

Abbreviations: BrW = brain weight; LW = liver weight; BtW = birth body weight in kg; EE = distance in pixels between the lateral edge of the ears, seen from above; Bt = area in pixels of the front head delimited by a square, seen from above; EE2 = distance in pixels between the medial edge of the ears, seen from above; Lt = area in pixels of the body delimited by a square from the caudal edge of the head to the caudal edge of the body, seen from above; L = area in pixels of the body delimited by a square from the caudal edge of the head to the caudal edge of the abdomen, seen from the side; Le = length of the body in pixels, from the caudal edge of the head to the end of the body following the spine, seen from above.

¹ P-value of r.
² BrW_{CT}/LW_{CT}~BtW+EE+L = brain-to-liver weight ratio predicted according to the first approach. An equation was constructed on the training dataset to estimate the BrW_{CT}/LW_{CT} by incorporating the distance between the lateral edges of the ears (EE) and the area of the body delimited by a square from the caudal edge of the head to the caudal edge of the abdomen (L), along with the BtW. These were the measures that better predicted the BrW_{CT} and LW_{CT}.
³ BrW_{CT}/LW_{CT}~BtW+EE+L (BtW>800 g) = brain-to-liver weight ratio predicted according to the first approach. An equation was constructed on the training dataset to estimate the BrW_{CT}/LW_{CT} by incorporating the distance between the lateral edges of the ears (EE) and the area of the body delimited by a square from the caudal edge of the head to the caudal edge of the abdomen (L), along with the BtW. These were the measures that better predicted the BrW_{CT} and LW_{CT}. Piglets with a BtW<800 g were excluded from the calculation of r, MAE, MAPE.
⁴ BrW_{CT}~BtW+EE / LW_{CT}~BtW+L = brain-to-liver weight ratio predicted according to the second approach. The values of BrW_{CT} and LW_{CT} estimated with the equations developed in the training dataset, derived from EE in combination with BtW and L in combination with BtW, respectively, were directly employed to determine the BrW_{CT}/LW_{CT}.
⁵ BrW_{CT}~BtW+EE / LW_{CT}~BtW+L (BtW>800 g) = brain-to-liver weight ratio predicted according to the second approach. The values of BrW_{CT} and LW_{CT} estimated with the equations developed in the training dataset, derived from EE in combination with BtW and L in combination with BtW, respectively, were directly employed to determine the BrW_{CT}/LW_{CT}. Piglets with a BtW<800 g were excluded from the calculation of r, MAE, MAPE.
⁶ BrW_{CT}/LW_{CT}~BtW = brain-to-liver weight ratio predicted according to the first approach but using the BtW as sole predictor. An equation was constructed on the training dataset to estimate the BrW_{CT}/LW_{CT} by incorporating only the BtW as independent variable.
⁷ BrW_{CT}/LW_{CT}~BtW (BtW>800 g) = brain-to-liver weight ratio predicted according to the first approach but using the BtW as sole predictor. An equation was constructed on the training dataset to estimate the BrW_{CT}/LW_{CT} by incorporating only the BtW as independent variable. Piglets with a BtW<800 g were excluded from the calculation of r, MAE, MAPE.
⁸ BrW_{CT}~BtW / LW_{CT}~BtW = brain-to-liver weight ratio predicted according to the second approach but using the BtW as sole predictor. The values of BrW_{CT} and LW_{CT} estimated with the equations developed in the training dataset incorporating only the BtW as independent variable, were directly employed to determine the BrW_{CT}/LW_{CT}.
⁹ BrW_{CT}~BtW / LW_{CT}~BtW (BtW>800 g) = brain-to-liver weight ratio predicted according to the second approach but using the BtW as sole predictor. The values of BrW_{CT} and LW_{CT} estimated with the equations developed in the training dataset incorporating only the BtW as independent variable, were directly employed to determine the BrW_{CT}/LW_{CT}. Piglets with a BtW<800 g were excluded from the calculation of r, MAE, MAPE.

ments. Our findings support the hypothesis that certain morphometric traits can serve as indicators of brain and liver weights, as well as their ratio. Using the distance between the ears (EE), in combination with the BtW, the BrW could be predicted with an error of 6%. Notably, the studies conducted by [Amdi et al. \(2013\)](#) and [Hansen et al. \(2018\)](#) postulated that if the relative BrW of a newborn piglet is below 3% of its BtW, the piglet can be diagnosed as normal. If this statement is true, the BrW estimated with the present equation could be simply compared with the piglet's BtW, enabling accurate and non-invasive identification of normal piglets with a narrow margin of error. It would also offer insights into piglets with a relative BrW above 3% of their BtW which might have suffered growth restriction in the uterus.

The LW was highly correlated with most of the collected morphometric traits. However, when using these measurements along

with the BtW in the prediction models, the error rate could not be reduced below 17%. As the actual LW_{CT} increased, the accuracy of the predictions worsened. This suggests that beyond a certain weight of the liver, the body's structure may no longer be associated with the organ's weight, unlike what was observed with the brain.

When we employed a combination of measures (BtW, EE, and L) that better predicted the BrW and the LW for estimating the BrW/LW, an error rate of 17% was observed. Using the second approach, in which the BrW and LW predicted with the previous models were directly employed to determine the BRW/LW, we observed a slight increase in the error rate to 20%. This outcome is likely attributable to the cumulative impact of errors encountered when predicting the weights of both organs. However, the BrW/LW allows for consideration of the different levels of growth restrictions that piglets may be exposed to during gestation. With a r up to 0.88 (according

Table 9

r, P-value of r, mean absolute error (MAE), mean absolute percentage error (MAPE), RMSE, RMSE % and coefficient of correlation and concordance (CCC) between true and predicted brain weight (BrW_{CT}), liver weight (LW_{CT}), and brain-to-liver weight ratio (BrW_{CT}/LW_{CT}) of the piglets in the testing dataset.

Item	r	P-value ¹	MAE	MAPE	RMSE	RMSE %	CCC
BrW _{CT}							
BrW _{CT} ~BtW+EE	0.84	< 0.001	1.95	0.06	2.32	7.05	0.83
BrW _{CT} ~BtW+Bt	0.83	< 0.001	1.99	0.06	2.39	7.26	0.82
BrW _{CT} ~BtW+EE2	0.82	< 0.001	2.07	0.07	2.47	7.49	0.82
BrW _{CT} ~BtW	0.80	< 0.001	2.17	0.07	2.56	7.77	0.80
LW _{CT}							
LW _{CT} ~BtW+Lt	0.91	< 0.001	9.35	0.24	11.5	22.9	0.89
LW _{CT} ~BtW+L	0.90	< 0.001	9.29	0.17	13.0	25.9	0.84
LW _{CT} ~BtW+Le	0.89	< 0.001	9.00	0.18	12.1	24.1	0.84
LW _{CT} ~BtW	0.89	< 0.001	8.73	0.18	12.0	23.8	0.85
BrW _{CT} /LW _{CT}							
BrW _{CT} /LW _{CT} ~BtW+EE+L ²	0.85	< 0.001	0.14	0.17	0.22	26.6	0.77
BrW _{CT} /LW _{CT} ~BtW+EE+L (BtW>800 g) ³	0.79	< 0.001	0.11	0.18	0.13	15.8	0.78
BrW _{CT} ~BtW+EE / LW _{CT} ~BtW+L ⁴	0.88	< 0.001	0.14	0.20	0.19	23.6	0.83
BrW _{CT} ~BtW+EE / LW _{CT} ~BtW+L (BtW>800 g) ⁵	0.75	< 0.001	0.12	0.21	0.14	17.4	0.71
BrW _{CT} /LW _{CT} ~BtW ⁶	0.83	< 0.001	0.15	0.18	0.23	27.9	0.74
BrW _{CT} /LW _{CT} ~BtW (BtW>800 g) ⁷	0.72	< 0.001	0.11	0.19	0.15	17.9	0.72
BrW _{CT} ~BtW / LW _{CT} ~BtW ⁸	0.87	< 0.001	0.14	0.18	0.22	26.8	0.77
BrW _{CT} ~BtW / LW _{CT} ~BtW (BtW>800 g) ⁹	0.69	< 0.001	0.11	0.18	0.14	17.6	0.64

Abbreviations: BrW = brain weight; LW weight; BtW = birth body weight in kg; EE = distance in pixels between the lateral edge of the ears, seen from above; Bt = area in pixels of the front head delimited by a square, seen from above; EE2 = distance in pixels between the medial edge of the ears, seen from above; Lt = area in pixels of the body delimited by a square from the caudal edge of the head to the caudal edge of the body, seen from above; L = area in pixels of the body delimited by a square from the caudal edge of the head to the caudal edge of the abdomen, seen from the side; Le = length of the body in pixels, from the caudal edge of the head to the end of the body following the spine, seen from above.

¹ P-value of r.
² BrW_{CT}/LW_{CT}~BtW+EE+L = brain-to-liver weight ratio predicted according to the first approach. An equation was constructed on the training dataset to estimate the BrW_{CT}/LW_{CT} by incorporating the distance between the lateral edges of the ears (EE) and the area of the body delimited by a square from the caudal edge of the head to the caudal edge of the abdomen (L), along with the BtW. These were the measures that better predicted the BrW_{CT} and LW_{CT}.
³ BrW_{CT}/LW_{CT}~BtW+EE+L (BtW>800 g) = brain-to-liver weight ratio predicted according to the first approach. An equation was constructed on the training dataset to estimate the BrW_{CT}/LW_{CT} by incorporating the distance between the lateral edges of the ears (EE) and the area of the body delimited by a square from the caudal edge of the head to the caudal edge of the abdomen (L), along with the BtW. These were the measures that better predicted the BrW_{CT} and LW_{CT}. Piglets with a BtW<800 g were excluded from the calculation of r, MAE, MAPE.
⁴ BrW_{CT}~BtW+EE / LW_{CT}~BtW+L = brain-to-liver weight ratio predicted according to the second approach. The values of BrW_{CT} and LW_{CT} estimated with the equations developed in the training dataset, derived from EE in combination with BtW and L in combination with BtW, respectively, were directly employed to determine the BrW_{CT}/LW_{CT}.
⁵ BrW_{CT}~BtW+EE / LW_{CT}~BtW+L (BtW>800 g) = brain-to-liver weight ratio predicted according to the second approach. The values of BrW_{CT} and LW_{CT} estimated with the equations developed in the training dataset, derived from EE in combination with BtW and L in combination with BtW, respectively, were directly employed to determine the BrW_{CT}/LW_{CT}. Piglets with a BtW<800 g were excluded from the calculation of r, MAE, MAPE.
⁶ BrW_{CT}/LW_{CT}~BtW = brain-to-liver weight ratio predicted according to the first approach but using the BtW as sole predictor. An equation was constructed on the training dataset to estimate the BrW_{CT}/LW_{CT} by incorporating only the BtW as independent variable.
⁷ BrW_{CT}/LW_{CT}~BtW (BtW>800 g) = brain-to-liver weight ratio predicted according to the first approach but using the BtW as sole predictor. An equation was constructed on the training dataset to estimate the BrW_{CT}/LW_{CT} by incorporating only the BtW as independent variable. Piglets with a BtW<800 g were excluded from the calculation of r, MAE, MAPE.
⁸ BrW_{CT}~BtW / LW_{CT}~BtW = brain-to-liver weight ratio predicted according to the second approach but using the BtW as sole predictor. The values of BrW_{CT} and LW_{CT} estimated with the equations developed in the training dataset incorporating only the BtW as independent variable, were directly employed to determine the BrW_{CT}/LW_{CT}.
⁹ BrW_{CT}~BtW / LW_{CT}~BtW (BtW>800 g) = brain-to-liver weight ratio predicted according to the second approach but using the BtW as sole predictor. The values of BrW_{CT} and LW_{CT} estimated with the equations developed in the training dataset incorporating only the BtW as independent variable, were directly employed to determine the BrW_{CT}/LW_{CT}. Piglets with a BtW<800 g were excluded from the calculation of r, MAE, MAPE.

to the different methods), the estimated BrW/LW is highly correlated with the true BrW/LW. Accordingly, the estimated BrW/LW can be used to assess the general tendency of an increase in BrW/LW for different traits, as analysed by Ruggeri et al. (2024).

Surprisingly, the error rates for predicting BrW, LW, and BrW/LW were comparable or, in some cases, even lower when BtW was used as the sole predictor rather than in conjunction with morphometric traits. However, ANOVA testing was used to systematically compare models that relied exclusively on BtW as a predictor with those that incorporated BtW alongside morphometric traits. The results suggest that incorporating each morphometric trait alongside BtW leads to a significant enhancement in model fit, thereby improving the predictive abilities of the models for BrW, LW, and BrW/LW. The only exception was noted with the variable Bt when predicting BrW. Furthermore, in the testing dataset, the correlation coefficients between the true and predicted values for BrW, LW, and BrW/LW were consistently higher when BtW

was used in combination with morphometric traits compared to using BtW alone, except for Le. These findings are noteworthy because, although models incorporating morphometric traits alongside BtW showed improved performance compared to those using BtW alone, the latter still demonstrated satisfactory predictive accuracy. Moreover, the ease of measuring the BtW of newborn piglets makes it a practical and accessible method in real-world applications. The euthanasia of piglets born with a BtW below 800 g is a common practice in modern swine production systems, primarily due to the high mortality rate observed among these piglets during the 1st days after birth (Muns et al., 2016). We hypothesized that in cases of extremely low BtWs, the association between organ weight and body morphology may weaken. When these piglets were excluded from the analysis, there was a reduction in the percentage error between actual and predicted BrW_{CT}/LW_{CT} in the training set. However, this reduction did not translate to the testing set, where excluding these piglets slightly increased

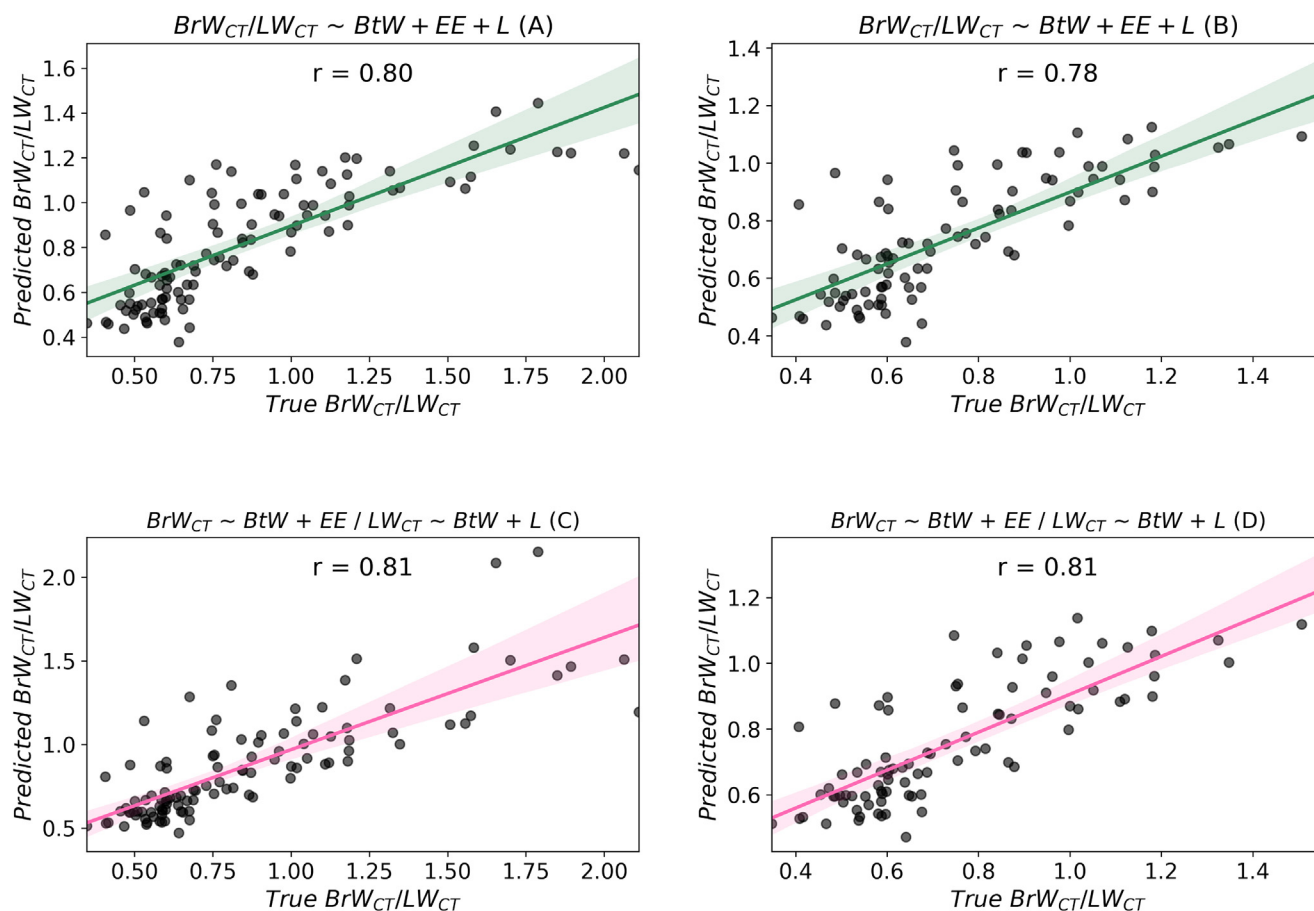


Fig. 8. Linear regressions between true and predicted BrW_{CT}/LW_{CT} of the piglets of the training dataset according to the first approach (panels A and B) and the second approach (panels C and D). Panel A and C: all population; panel B and D: piglets with a birth weight (BtW) above 800 g. x-Axis: true brain-to-liver weight ratio (true BrW_{CT}/LW_{CT}); y-axis: predicted brain-to-liver weight ratio (predicted BrW_{CT}/LW_{CT}). In the first approach, the two variables which, along with the BtW, better predicted the BrW_{CT} and LW_{CT} were used in combination to develop a multiple linear regression model to predict the BrW_{CT}/LW_{CT} . The regression model included the BtW expressed in kg, the distance in pixels between the lateral edge of the ears, seen from above (EE), and the area in pixels of the body delimited by a square from the caudal edge of the head to the caudal edge of the abdomen, seen from the side (L). In the second approach, the predicted BrW_{CT} and LW_{CT} , calculated using the previous models ($BrW_{CT} \sim BtW + EE$; $LW_{CT} \sim BtW + L$), were directly employed to determine the BrW_{CT}/LW_{CT} .

the percentage error. A possible explanation for the increased MAPE in the testing set after excluding piglets with a BtW below 800 g may be that the number of samples in the testing set dropped below 30. This reduction in sample size could have resulted in unreliable predictions due to statistical instability or insufficient representation of the population (Jenkins and Quintana-Ascencio, 2020; Austin and Steyerberg, 2015).

In this study, to ensure the repeatability of the method, a subset of the morphometric traits was taken by a second observer. The measurements taken by the authors and the second observer were highly correlated, reinforcing the consistency and accuracy of the identified morphometric traits to estimate BrW and LW. This correlation validates the method and shows that the results are not solely a consequence of subjective measurement but rather are indicative of a link between these morphometric traits and the BrW and LW.

In addition, the division of the dataset into training and testing subsets was helpful in evaluating the ability of the predictive models to generalize on new data. By creating a clear division between

training and testing data, the study replicates the real-world scenario where predictive models are applied to new, unseen observations. This evaluation mechanism protects against overfitting, a situation where the models become overly specialized to the training data and may perform poorly when exposed to new inputs (Hawkins, 2004).

Conclusion

In conclusion, this study demonstrates the potential of using body measurements as non-invasive indicators of the brain-to-organ weight ratio for diagnosing IUGR in newborn piglets. The developed predictive models provide a promising tool for the early identification of IUGR piglets, facilitating timely interventions and improved management strategies. Future studies should focus on validating these models in larger populations and different breeds. Furthermore, it is essential to explore their applicability under field conditions and to develop techniques for automating the extraction of morphometric traits from images. The successful imple-

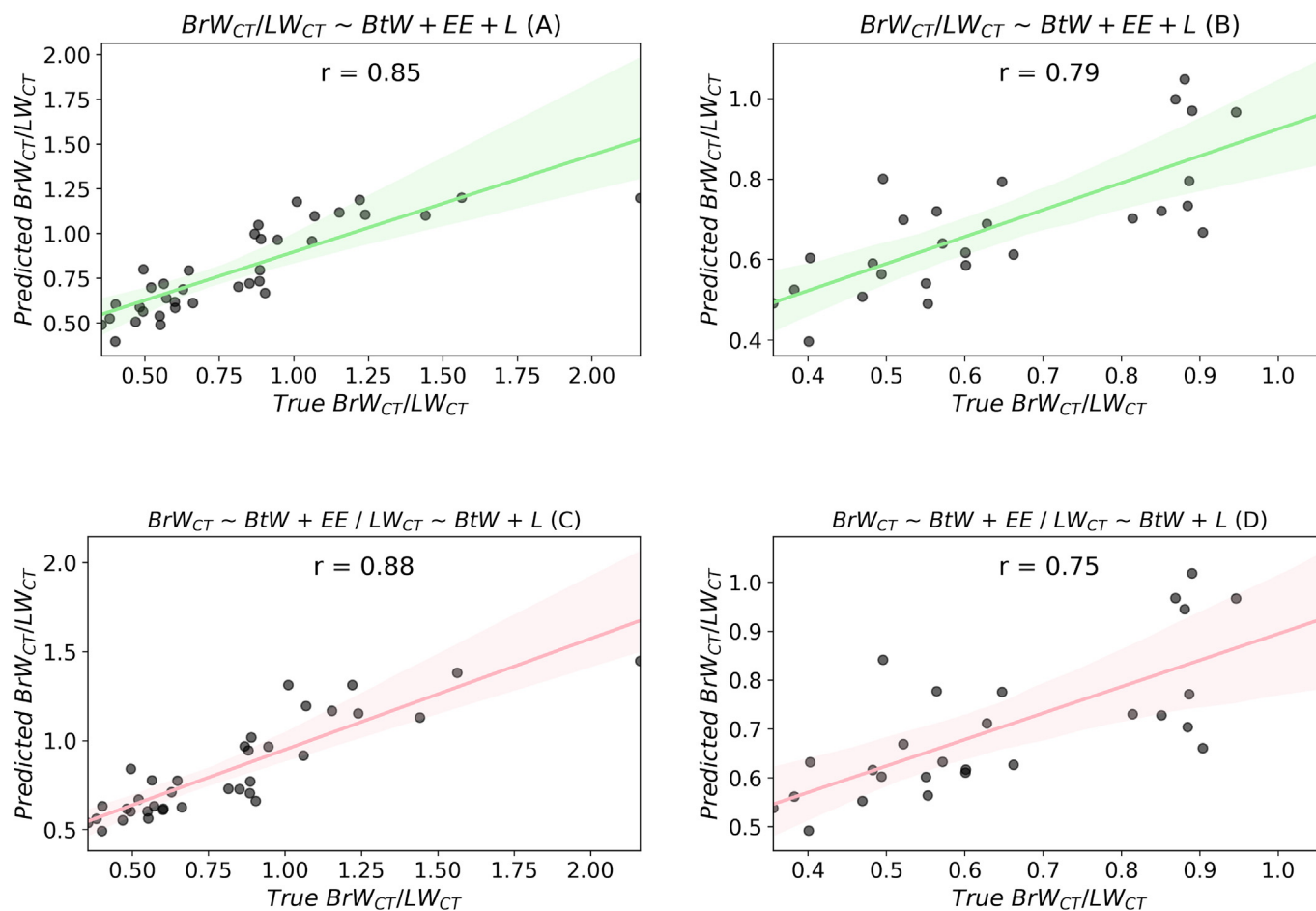


Fig. 9. Linear regressions between true and predicted BrW_{CT}/LW_{CT} of the piglets of the testing dataset according to the first approach (panels A and B) and the second approach (panels C and D). Panels A and C: all population; panels B and D: piglets with a birth weight (BtW) above 800 g. x-Axis: true brain-to-liver weight ratio (true BrW_{CT}/LW_{CT}); y-axis: predicted brain-to-liver weight ratio (predicted BrW_{CT}/LW_{CT}). In the first approach, the two variables which, along with the BtW, better predicted the BrW_{CT} and LW_{CT} were used in combination to develop a multiple linear regression model to predict the BrW_{CT}/LW_{CT} . The regression model included the BtW expressed in kg, the distance in pixels between the lateral edge of the ears, seen from above (EE), and the area in pixels of the body delimited by a square from the caudal edge of the head to the caudal edge of the abdomen, seen from the side (L). In the second approach, the predicted BrW_{CT} and LW_{CT} , calculated using the previous models ($BrW_{CT} \sim BtW + EE$; $LW_{CT} \sim BtW + L$), were directly employed to determine the BrW_{CT}/LW_{CT} .

mentation of such non-invasive diagnostic approaches will contribute to the welfare and productivity of pig production systems.

Supplementary material

Supplementary material to this article can be found online at <https://doi.org/10.1016/j.animal.2024.101262>.

Ethics approval

The experiments were performed at the Agroscope research institute, Posieux (Switzerland). All the experimental procedures complied with Swiss animal welfare guidelines and were approved (experimental approval numbers 32751 and 35131) by the Cantonal Veterinary Office of Fribourg (Switzerland).

Data and model availability statement

The data that support the findings of this study were not deposited in an official repository but are available upon reasonable request from the corresponding author.

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the author(s) used ChatGPT (OpenAI, 2023) in order to verify the statistical analysis and review the English writing. After using this tool/service, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the publication.

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Writing – review & editing. **C. Ollagnier:** Writing – review & editing, Supervision, Investigation, Formal analysis, Conceptualization.

Declaration of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Annex 1. Equations

1. $BrD_{Eu} = BrW_{Eu} / BrV_{Eu}^1$
2. $LD_{Eu} = LW_{Eu} / LV_{Eu}^2$
3. $BrW_{CT} = BrD_{Eu} \times BrV_{CT}^3$
4. $LW_{CT} = LD_{Eu} \times LV_{CT}^4$

References

- Amdt, C., Krogh, U., Flummer, C., Oksbjerg, N., Hansen, C.F., Theil, P.K., 2013. Intrauterine growth restricted piglets defined by their head shape ingest insufficient amounts of colostrum. *Journal of Animal Science* 91, 5605–5613.
- Amdt, C., Lynegaard, J.C., Thymann, T., Williams, A.R., 2020. Intrauterine growth restriction in piglets alters blood cell counts and impairs cytokine responses in peripheral mononuclear cells 24 days post-partum. *Scientific Reports* 10, 4683.
- Austin, P.C., Steyerberg, E.W., 2015. The number of subjects per variable required in linear regression analyses. *Journal of Clinical Epidemiology* 68, 627–636.
- Bauer, R., Walter, B., Brust, P., Füchtner, F., Zwiener, U., 2003. Impact of asymmetric intrauterine growth restriction on organ function in newborn piglets. *European Journal of Obstetrics & Gynecology and Reproductive Biology* 110, S40–S49.
- Campos, P.H.R.F., Silva, B.A.N., Donzele, J.L., Oliveira, R.F.M., Knol, E.F., 2012. Effects of sow nutrition during gestation on within-litter birth weight variation: a review. *Animal* 6, 797–806.
- Chand, K.K., Pannek, K., Colditz, P.B., Wixey, J.A., 2022. Brain outcomes in runt piglets: a translational model of fetal growth restriction. *Developmental Neuroscience* 44, 194–204.

- Cohen, E., Baerts, W., van Bel, F., 2015. Brain-sparing in intrauterine growth restriction: considerations for the neonatologist. *Neonatology* 108, 269–276.
- De Vos, M., Che, L., Huygelen, V., Willems, S., Michiels, J., Van Cruchten, S., Van Ginneken, C., 2014. Nutritional interventions to prevent and rear low-birthweight piglets. *Journal of Animal Physiology and Animal Nutrition* 98, 609–619.
- D'Inca, R., Che, L., Thymann, T., Sangild, P.T., Le Huërou-Luron, I., 2010. Intrauterine growth restriction reduces intestinal structure and modifies the response to colostrum in preterm and term piglets. *Livestock Science* 133, 20–22.
- Felicioni, F., Santos, T.G., e Paula, T.D.M.D., Chiarini-Garcia, H., de Almeida, F.R.C.L., 2019. Intrauterine growth restriction: screening and diagnosis using animal models. *Animal Reproduction* 16, 66.
- Gupta, M., 2008. Intrauterine growth restriction. In: Brodsky, D., Ouellette, M.A. (Eds.), *Primary Care of the Premature Infant*. W.B. Saunders, Philadelphia, PA, USA, pp. 77–83.
- Hales, J., Moustsen, V.A., Nielsen, M.B.F., Hansen, C.F., 2013. Individual physical characteristics of neonatal piglets affect preweaning survival of piglets born in a non-crated system. *Journal of Animal Science* 91, 4991–5003.
- Hansen, C.F., Hales, J., Amdt, C., Moustsen, V.A., 2018. Intrauterine growth-restricted piglets defined by their head shape have impaired survival and growth during the suckling period. *Animal Production Science* 59, 1056–1062.
- Hawkins, D.M., 2004. The problem of overfitting. *Journal of Chemical Information and Computer Sciences* 44, 1–12.
- Huting, A.M.S., Sakkas, P., Wellock, I., Almond, K., Kyriazakis, I., 2018. Once small always small? To what extent morphometric characteristics and post-weaning starter regime affect pig lifetime growth performance. *Porcine Health Management* 4, 1–14.
- Jenkins, D.G., Quintana-Ascencio, P.F., 2020. A solution to minimum sample size for regressions. *PloS ONE* 15, e0229345.
- Lemke, A.J., Brinkmann, M.J., Schott, T., Niehues, S.M., Settmacher, U., Neuhaus, P., Felix, R., 2006. Living donor right liver lobes: preoperative CT volumetric measurement for calculation of intraoperative weight and volume. *Radiology* 240, 736–742.
- Muns, R., Nuntapaitoon, M., Tummaruk, P., 2016. Non-infectious causes of preweaning mortality in piglets. *Livestock Science* 184, 46–57.
- Quiniou, N., Dagorn, J., Gaudré, D., 2002. Variation of piglets' birth weight and consequences on subsequent performance. *Livestock Production Science* 78, 63–70.
- Ruggeri, R., Bee, G., Trevisi, P., Ollagnier, C., 2024. Intrauterine growth restriction defined by increased brain-to-liver weight ratio affects postnatal growth and protein efficiency in pigs. *Animal* 18, 101044.
- Santos, T. G., S. D. Fernandes, S. B. de Oliveira Araújo, F. Felicioni, T. de Mérici Domingues e Paula, A. L. Caldeira-Brant, S. V. Ferreira, L. de Paula Naves, S. P. de Souza and P. H. R. F., Campos, 2022. Intrauterine growth restriction and its impact on intestinal morphophysiology throughout postnatal development in pigs. *Scientific Reports* 12, 11810.
- Van Ginneken, C., Ayuso, M., Van Bockstal, L., Van Cruchten, S., 2023. Preweaning performance in intrauterine growth-restricted piglets: characteristics and interventions. *Molecular Reproduction and Development* 90, 697–707.
- Wang, W., Degroote, J., Van Ginneken, C., Van Poucke, M., Vergauwen, H., Dam, T.M. T., Vanromp, D., Peelman, L.J., De Smet, S., Michiels, J., 2016. Intrauterine growth restriction in neonatal piglets affects small intestinal mucosal permeability and mRNA expression of redox-sensitive genes. *The FASEB Journal* 30, 863–873.
- Wu, G., Bazer, F.W., Wallace, J.M., Spencer, T.E., 2006. Board-invited review: intrauterine growth retardation: implications for the animal sciences. *Journal of Animal Science* 84, 2316–2337.

¹ BrD_{Eu} = brain density; BrW_{Eu} = brain weight in g measured with a scale on 30 piglets after euthanasia; BrV_{Eu} = brain volume in mL measured with the water displacement method on 30 piglets after euthanasia.

² LD_{Eu} = liver density; LW_{Eu} = liver weight in g measured with a scale on 30 piglets after euthanasia; LV_{Eu} = liver volume in mL measured with the water displacement method on 30 piglets after euthanasia.

³ BrW_{CT} = brain weight; BrD_{Eu} = brain density calculated on 30 piglets after euthanasia; BrV_{CT} = brain volume in mL measured with computed tomography (CT) scan.

⁴ LW_{CT} = liver weight; LD_{Eu} = liver density calculated on 30 piglets after euthanasia; LV_{CT} = liver volume in mL measured with computed tomography (CT) scan.