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**TRABALHO FINAL**
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Laboratório de Nutrição

# How to assess and interpret Phase Angle in Cancer: The Clinical Relevance

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# How to assess and interpret Phase Angle in Cancer: The Clinical Relevance

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**Orientado por:**

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## ABSTRACT

It is widely known that nutritional deterioration in cancer patients is a strong predictor of patients' treatment outcome and survival. To clarify this association, there is an increasing use of bioelectrical impedance analysis (BIA) to evaluate body composition and phase angle (PhA) in cancer. The aims of this review were: 1) to explore the efficacy of BIA for body composition analysis in cancer; 2) to determine the value of the implementation of BIA for evaluating outcomes in cancer in clinical practice and 3) to evaluate the relevance of assessing phase angle in oncology practice. PubMed, MedLine, CINAHL, EBSCO and Cochrane Library have been searched for relevant publications in English, until March 2017. The keywords used were "cancer", "phase angle", "body composition", "BIA", "outcomes". Original research studies were thoroughly reviewed to identify strengths and limitations, to enable a better understanding of the mechanisms and support the use of BIA in the routine evaluation of cancer patients. The use of BIA and its derived parameters, most importantly PhA and body cell mass, provide practitioners with a sensitive, convenient, and non-invasive method for the evaluation of nutritional status, body cell mass and overall health status in cancer patients. BIA can assist practitioners in the evaluation of nutritional deterioration and risk of cachexia. PhA indicates indirectly the integrity of cell membrane, and thus potentially disease progression. The implementation of these parameters given by BIA should be encouraged as they may allow for timely adjustments of treatment regimens, and appropriate nutrition and medical intervention to improve Quality of Life and eventually prognosis.



Keywords : "cancer", "phase angle", "body composition", "BIA", "outcomes"


The final work expresses the opinion of the author and not the FML's opinion.

## RESUMO

É globalmente conhecido que a deterioração nutricional em doentes oncológicos é um forte preditor do potencial resultado de um tratamento e de sobrevivência. Para clarificar esta associação, existe um incremento no uso da Análise Bioeléctrica por Bioimpedância (ABB) para avaliar a composição corporal e o ângulo de fase (AF) em oncologia. Os objectivos desta revisão são: 1) determinar o valor da implementação da ABB para avaliar o resultado em oncologia e na prática clínica; 2) determinar a relevância de avaliar o AF na prática clínica em oncologia. PubMed, MedLine, CINAHL, EBSCO e Cochrane foram pesquisadas com o propósito de seleccionar publicações relevantes em Inglês e publicadas até Março de 2017. As palavras chave foram "cancro", "ângulo de fase", "composição corporal", "ABB" e "resultados". Vários artigos científicos foram completamente revistos como intuíto de identificar os pontos fortes e fracos dos mesmos , para permitir assim uma melhor compreensão dos mecanismos que possam validar o uso de ABB numa avaliação rotineira de doentes oncológicos. O uso de ABB e seus derivados, principalmente o AF e massa celular, fornece aos clínicos um método sensivel, não-invasivo e conveniente para a avaliação nutricional destes doentes. ABB pode assim apoiar os clínicos numa avaliação de uma possível deterioração nutricional e risco de caquéxia. O AF indica inderectamente a integridade da membrana celular  e assim possivelmente a progressão da doença. A implementação destes parâmetros deve ser encorajada pois podem permitir ajustes em regimes terapêuticos e aporte nutricional. Promovendo assim uma possível melhor qualidade de vida e prognóstico.



Palavras chave: "cancro", "ângulo de fase", "composição corporal", "ABB" e "resultados"

# INDEX

# INTRODUTION

Undernutrition is consistently associated with cancer; in fact, historically through times until nowadays, weight loss is significantly incident among cancer patients and it does dictate a poorer tolerance to antineoplastic treatments and a shorter survival (Dewys et al, 1980). Although its recognition as a strong prognostic predictor, undernutrition is still under-diagnosed and under-assessed in clinical practice and therefore under-treated or even untreated. Notwithstanding, in Oncology as is other patient' populations, recent data show that nutritional status may range from undernutrition to excess body weight to obesity (Ravasco et al, 2010). This occurs due to the high prevalence of overweight/obesity in western countries; this contributes to a high proportion of cancer patients with inadequate body mass index (BMI), e.g. $\geq$25kg/m$^2$. Recent studies from our group show a prevalence of 63% of overweigh/obesity in several cancer types, especially of the breast, prostate, gynecological and colon-rectum (Ravasco et al, 2010). Nevertheless, overweight/obesity does not overrule sarcopenia that may be concomitantly present; this new scenario of sarcopenic obesity has been consistently associated with a poor disease prognosis, since it may determine lower functional status, higher toxicity to antineoplastic treatments and lower survival (Martin et al, 2013).

Due to this diverse and new scenario in Oncology, new methods and techniques to assess nutritional status and body composition have been explored. Computerized Tomography (CT) scans at the level of the third lumbar vertebrae have recently been validated in Oncology to determine the quantity of body muscle and of fat mass. Moreover, CT scans also allow the verification of fat infiltration into muscle fibers (muscle attenuation); this parameter indicates that muscle contraction may be compromised, which translates in patients' lower functional status. As already mentioned, another method for body composition assessment that may be integrated in clinical practice is BIA (Kyle et al, 2004), which is simple and quick, and provides data on fat mass, lean body mass, body fluid distribution and phase angle. PhA is an objective parameter that may indicate body tissues' electric properties and therefore, cellular health and its metabolic performance (Gupta et al, 2008). It is thus considered not only a potential indicator of nutritional status, but also an indicator of overall disease status and prognosis.

The present review will focus on the clinical value of PhA given by BIA for nutritional, metabolic and clinical assessment of cancer patients, and the potential

applicability in routine practice in the Oncology setting. For that we will 1) explore the potential significance of BIA for body composition analysis in cancer; 2) to determine the value of the implementation of BIA for evaluating outcomes in cancer in clinical practice and 3) to evaluate the relevance of assessing phase angle in oncology practice.

## BIOELECTRICAL IMPEDANCE ANALYSIS (BIA)

BIA is a non-invasive, easy-to-use, reproducible method, which can be conducted at the bedside (Kyle et al, 2004; Norman et al, 2012). Its principles are based on: 1) the passage of a very low voltage electric current through the body and 2) on the ability of the different body tissues' conduction related with the electrical properties of tissues. Deriving from the resistance of the body cells to the passage of the electrical current, two values are obtained: Resistance (*R*) and Reactance (*Xc*): *R* is the opponent to the flow of an alternating electrical current through intracellular and extracellular ionic solutions, and *Xc* is the expression of the bioelectric properties of cell membranes and tissues' interfaces (Paiva et al, 2011). The combination of resistance and reactance is called Impedance. The electric current passes mainly through tissues with high water content (fat-free mass - FFM) since bone and fat mass (FM) have high impedance, which determines a reduced conduction of the electric current (Norman et al, 2008).

Both *R* and *Xc* may be measured at different frequencies, ranging from zero to an infinite frequency. At zero frequency, the electric current passes exclusively through the extracellular fluid, while at an infinite frequency, the current penetrates the cell membrane reflecting both intracellular and extracellular fluid (Paiva et al, 2011; Norman et al, 2008). Most single-frequency BIA equipments operate at a frequency of 50 kHz, which promotes the passage of the electric current through intra and extra cellular fluid at different proportions, depending on the penetrated tissue. Single-frequency BIA measures FFM and total body water (TBW), but it does not distinguish between intra (ICW) and extracellular water (ECW). Multi-frequency BIA devices can determine FFM, TBW, ICW and ECW (Kyle et al, 2004).

In order to obtain body composition, impedance values need to be converted by means of validated equations that are specific to certain populations according to age, sex and ethnicity. Altered tissue conductivity and/or abnormal tissue hydration may result in incorrect body composition analysis by BIA, since validated equations for healthy populations may be inadequate for ill/hospitalized individuals (Paiva et al, 2011). Of note that BIA equations are

not able to predict body composition in patients with a BMI >34kg/m$^2$ given the abnormal hydration, increased fat content and altered geometric tissue distribution. Therefore, in patients with chronic diseases, altered fluid balance and morbid obesity, BIA accuracy may be compromised; future validation studies are needed in order to evaluate BIA validity in these specific populations (Tisdale, 2010; Toso et al, 2000).

## PHASE ANGLE

PhA is the relationship between raw impedance values: *R* and *Xc*, and it is calculated with the formula: arc tangent $\frac{Xc}{R} \times \frac{180^o}{\pi}$. Subsequently, PhA has a clear advantage other BIA parameters, since it does not rely neither on regression predictive equations for body composition, nor on the assumption of a constant tissue hydration. Recently, PhA research has attained major interest since it seems to be a potential predictor of poor clinical outcome and mortality in various pathologies and clinical conditions, e.g. HIV, AIDS, hemodialysis, liver cirrhosis and cancer (Tisdale, 2010). In disease states, fluid disturbance may occur, as well as loss of cell membrane integrity, leading to alterations in tissues conductivity (Toso et al, 2000; Toso et al, 2003). Given these structural changes, there may be altered impedance parameters since intra and extracellular fluid distribution is given by *R*, and cell membrane integrity is given by *Xc*. Ultimately, these changes are reflected on the PhA value, where lower values indicate poorer cell health, lower cellularity and loss of cell membrane integrity, reflecting worse cell function (Toso et al, 2000; Toso et al, 2003). Therefore, PhA expresses both the quality and quantity of soft tissues, being also suggested as a indicator of body cell mass (Gupta et al, 2004).

PhA is determined with 3 main factors: age, gender and BMI. With ageing, PhA tends to decrease because of loss of skeletal muscle that translates into a reduced body reactance; on the other hand, resistance may increase due to a reduction on water content concomitantly with an increase in fat mass (Paiva et al, 2011. In what concerns gender, PhA is higher in men than women due to a greater muscle mass compartment. As for BMI, it has been observed that PhA may increase in higher BMIs because of the higher number of cells (adipocytes or muscle cells) (Toso et al, 2000). However, this relationship was only observed for a BMI<30kg/m$^2$, whilst for a BMI >30kg/m$^2$–40kg/m$^2$ this relationship was not found and for

BMI >40Kg/$m^2$, an inverse correlation was found. This may be explained by a loss of integrity of cell membranes caused by pro-inflammatory cytokines secreted by adipocytes and/or because of a shift of fluid balance in morbid obesity, characterized by augmented extracellular/intracellular fluid ratio. Therefore, PhA reference values, standardized for age, gender and BMI are mandatory for PhA analysis (Gupta et al, 2004).

PhA has been explored as a potential indicator of undernutrition, functional status and disease prognosis in cancer. Interestingly, in disease-related malnutrition, electric properties of tissues may be disturbed leading to lower PhA; both a decrease in body cell mass in relation to extracellular mass, and an increase in the ratio extracellular/intracellular fluid may be reflected by PhA (Gupta et al, 2004; Gupta et al, 2004; Gupta et al, 2008). Furthermore, infection, inflammation or other clinical problems associated with a compromised health status, may all contribute to a low PhA which makes it a promising variable to take into consideration in cancer management, in nutrition and disease, clinical course and outcome.

## PHASE ANGLE: IMPACT ON CLINICAL OUTCOME

Some studies explored the potential prognostic value of PhA in cancer, namely on long term Quality of Life (QoL), functional status and survival (Gupta et al, 2004; Gupta et al, 2004; Gupta et al, 2008). The first studies that evaluated the impact of PhA on survival were retrospective and included patients with cancer of the colon-rectum, pancreas, breast and lung. The methodology was similar between studies: median PhA was used as the cut-off value within the study population. Patients with a PhA below the median value had a significantly lower survival *vs* patients with a PhA higher than the median value. In a study conducted in head-neck cancer patients in stages IIIB and IV, those whose PhA was <4,733º had a significantly higher risk for shortened overall survival *vs*. the remaining patients (19.6 months *vs*. 45 months) (Wladysiuk et al, 2016). Even though there was statistical significance in these findings, there are some limitations in their integration in the clinical setting: median PhA might not be applicable in other populations and it does not consider the three PhA determinants (age, gender and BMI). Therefore, improved methodology and study designs are mandatory to corroborate these findings: prospective studies and the PhA reference values should derive from healthy populations to assess the eventual deviation of PhA *vs* population

average values. In this sense, reference values were presented as percentiles standardized for PhA major determinants; Barbosa e Silva *et al* published PhA reference values for healthy Americans (n=1967 adults), stratified for age and gender. Later on, the reference values were published, stratified for age, gender and BMI, generated from a sample of 214,732 healthy German adults; to our knowledge these are the only PhA reference values stratified according to the three major PhA determinants (Gupta et al, 2009; Santarpia et al, 2009).

In order to overcome the previously mentioned limitations, Norman *et al* conducted a prospective study on 399 cancer patients with different tumours, to assess the prognostic value of PhA on nutritional status, muscle function, QoL and & months survival (Norman et al, 2010). The $5^{th}$ percentile was established as the cut-off and a new approach on PhA analysis was used; PhA values were standardized by creating a *z-score:* standardized PhA (SPhA)=(observed PhA–mean PhA)/SD PhA, in which mean and SD result from stratified values for age, gender and BMI. This approach did show that a PhA<$5^{th}$ percentile predicted a lower nutritional and functional status and an impaired QoL; moreover, it was also associated with a significantly higher 6 months mortality risk (OR: 4.0; 95% CI: 2.4, 6.8; p<0.001) and a 37.4% probability of death (Norman et al, 2010). On the other hand, SPhA emerged as an independent predictor of impaired muscle function, malnutrition and 6 months mortality, showing a better performance than malnutrition assessed by Subjective Global Assessment; thus, the authors concluded that SPhA improved the prognostic value of PhA, clearly due to its ability to assess and quantify patients' individual deviations from populations averages (Sanchez-Lara et al, 2012).

Other studies explored the prognostic value of PhA by estimating SPhA. Paiva *et al* conducted a prospective study in cancer patients with various tumours: breast, gynecological, gastrointestinal, head-neck (Paiva et al, 2011). A low PhA corresponded to the SPhA's $5^{th}$ percentile of the normal population; by using this cutoff, patients with a low SPhA had a relative risk of 3.25 for mortality *vs* a SPhA ≥$5^{th}$ percentile (Paiva et al, 2011). The use of a heterogeneous patient population including several tumour types and the lack of comparison with other prognostic factors may be a limitation of this study in what concerns assessing the value of PhA as a potential prognostic predictor. Subsequently, Urbain P *et al* published a prospective study in hematological cancer patients submitted to allogeneic hematopoietic cell transplantation, aiming to investigate the validity of several nutritional parameters, including SPhA, Subjective Global Assessment (SGA) and previous weight change as independent predictors of outcome until 2 years after transplantation (Sanchez-Lara K et al, 2012). The cut-off for a low PhA was defined as the $25^{th}$ quartile of the SPhA in the study population

calculated using gender-, age- and BMI-specific reference values for the German population. Results showed that PhA was an independent predictor for 2-year outcomes in these patients, having a superior performance than SGA and weight change' history (Sanchez-Lara K et al, 2012). Another approach was reports in a study that analyzed potential relationships between PhA and tumour volume in patients with non small cell lung cancer. The results supported the fact that tumour volumes were negatively correlated with PhA ($r=-0.55$; $p<0.001$), meaning that the PhA is closely associated with tumour burden for the host; this is of central importance to plan and prioritise early nutritional interventions, as it may indicate poor outcome at the time of diagnosis (Castanho et al, 2012).

Recently, our group also performed a pilot study including 71 patients with various cancers at various stages, referred for Radiotherapy. PhA was compared with reference values, stratified by age and gender, and the $5^{th}$ percentile of the reference population was established as the cut-off (data not shown). A low PhA was found in 16% of patients and of those, 90% had advanced disease (stages III/IV). Nutritional status by Patient Generated-Subjective Global Assessment (PG-SGA), showed that 37% of patients were undernourished (moderately/severely). By crossing variables we found that 91% of patients with low PhA were undernourished ($p<0.001$) and had indication for urgent nutritional intervention. The PG-SGA score that indicates the need for nutritional intervention was stratified according to the $5^{th}$ percentile of PhA; results showed that patients with a PhA $<5^{th}$ percentile had a significantly higher total PG-SGA score than those with a PhA $>5^{th}$ percentile [median: 10 IQ (7-17) *vs* median: 5 IQ (2-7), $p=0.002$]. In addition, QoL was also evaluated by the European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire, version 3.0 (EORTC-QLQ C30). PhA's $5^{th}$ percentile did anticipate a poorer global health perception ($p=0.008$) and global QoL scores ($p=0.02$); moreover, impaired physical, role and social functions were also found ($p<0.05$), as well as worse symptoms, e.g. fatigue, nausea and vomiting, anorexia and sleep disturbances ($p<0.05$). Based on our results, PhA may be useful to prioritize patients with critical need of nutritional intervention and for symptoms' management, in order to maintain or even improve patients' nutritional status, QoL and to optimize patients' tolerance to treatments and with this, their efficacy.

This year, a new study using multi-frequency evaluation was published with six different measures of PhA (5, 50 and 250 kHz in both sides of the body) in patients with advanced cancer. For all six PhA variables, a lower value was significantly associated with poorer overall survival ($p<0.001$). After adjusting for cancer type, performance status, weight loss and inflammatory markers, PhA remained independently associated with overall survival.

The authors concluded that regardless of the frequency and body sides, PhA represents an objective prognostic factor in the cancer care setting (Hui et al, 2017).

## PHASE ANGLE: FUTURE PERSPECTIVES

The potential prognostic predictor value of PhA in cancer is seemingly important; the literature shows its relevance and its value for integration in clinical practice as an easy variable to assess in patients, thus clinical researchers need to work on the limitations found in published studies for future ones. First, a consensus needs to be found on the cut-off that defines a low PhA. The SPhA calculation seems to be the most reliable approach to be used, since it not only compares PhA values with reference values from the healthy population, but also measures patients' individual deviation from a population average; however, the reviewed studies used different cut-offs to define a low PhA. While Paiva *et al* established a low PhA as the $5^{th}$ percentile value of the reference population, Urbain P defined a low PhA as the $1^{st}$ quartile of the sample population. In the later study, the authors did state that this cut-off was a study limitation, since the external validity of the results was compromised; thus, PhA values in this study were extremely low which did not allow the use of the $5^{th}$ percentile as the cut-off. This may indicate that PhA values may vary, not only between different cancer stages, but also between different types of cancer. Therefore, future research should focus on the identification of a valid cut-offs to be applied in clinical practice; these studies should be conducted in homogeneous populations, in order to evaluate potential differences of PhA values in different cancers.

Second the use of different BIA devices in between studies. Although Resistance and Reactance are raw impedance parameters, the impedance results may vary between different devices. Actually, PhA and *Xc* values have been compared between two different devices: Xitron 4000B® and Data Input BIA 2000S® and differences were found. Therefore, further investigation on the potential impact of BIA devices is required, in order to explore the need of impedance analyser-specific reference values, besides age, sex and BMI.

Third, PhA does seem promising as a prognostic predictor in cancer; yet there are no studies investigating the effect of specific therapies, either nutritional, pharmacological or life-style/physical activity on PhA values. It is important to establish that PhA expresses cellular health/function given by the cell membrane integrity and the balance between intra

and extracellular fluid, as well as by the quantity of body cell mass. Randomized trials with specific treatments and outcomes may modulate these cell and metabolic variables. Then, PhA assumes a major role for an early determination of favorable or unfavorable outcome of adjuvant therapies, allowing for timely corrections and adaptations with clear benefits for patients, QoL and overall disease prognosis.

The use of BIA and its derived parameters, most importantly Phase Angle and body cell mass, provide clinicians with a sensitive, non-invasive, easy to use method to evaluate body composition as well as overall health status in patients. BIA can assist practitioners in the evaluation of undernutrition, cachexia, disease progression, and cell metabolism and integrity, and based on this review, its use should be encouraged. The knowledge of all those parameters allow for adjustments in treatment regimens making them adequate and individualized, and therefore appropriate interventions to improve QoL and survival are a highly enthusiastic prospect.

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**Table 1.** Studies on phase angle and outcomes in cancer patients

| Authors | Population and study design | PhA and BIA device | Outcome | Results |
|---|---|---|---|---|
| **Gupta *et al* 2004** | 52 patients<br>Stage IV colorectal cancer<br>Retrospective study | Cut-off value: median PhA of study sample (5.57º)<br>BIA device: BIA-101Q (RJL Systems Inc.®) | Survival | Median survival in patients with PhA≤5.57 was lower (8.6 mo, 95% CI: 4.8, 12.4; n=26) than in patients with a PhA>5.57 (40.4 mo, 95% CI: 21.9, 58.8; n=26), p=0.0001. A PhA≤5.57 was associated with a relative risk increase of 10.75 (95% CI: 1.92, 60.24), p=0.007. |
| **Gupta *et al* 2004** | 58 patients<br>Stage IV pancreatic cancer<br>Retrospective study | Cut-off value: median PhA of the study sample (5.0)<br>BIA device: BIA-101Q (RJL Systems Inc.®) | Survival | Median survival in patients with PhA≤5.0 was lower (6.3 mo, 95% CI: 3.5, 9.2; n=29) than in patients with a PhA>5.0 (10.2 mo, 95% CI: 9.6, 10.8; n=29), p=0.02. Every one unit increase in PhA was associated with a relative risk of 0.69 (95% CI: 0.58, 0.96), p=0.02 |
| **Gupta *et al* 2008** | 259 patients<br>Breast cancer<br>Retrospective study | Cut-off value: median PhA of the study sample (5.6º)<br>BIA device: BIA-101Q (RJL Systems Inc.®) | Survival | Median survival in patients with PhA≤5.6 was lower (23.1 mo, 95% CI: 14.2, 31.9; n=129) than in patients with a PhA>5.6 (49.9 mo, 95% CI: 35.6, 77.8; n=130), p=0.031. Every one unit increase in PhA was associated with a relative risk |

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| | | | | of 0.82 (95% CI: 0.68, 0.99), p=0.041 |
| **Gupta *et al* 2009** | 165 patients<br>Stage IIIB+IV non-small cell lung cancer<br>Retrospective study | Cut-off value: median PhA of the study sample (5.3º)<br>BIA device: BIA-101Q (RJL Systems Inc.®) | Survival | Median survival in patients with PhA≤5.3 was lower (7.6 mo, 95% CI: 4.7, 9.5; n=81) than in patients with a PhA>5.3 (12.4 mo, 95% CI:10.5, 18.7; n=84), p=0.02. Every 1 degree increase in PhA was associated with a relative risk of 0.79 (95% CI: 0.64, 0.97), p=0.02 |
| **Norman *et al* 2010** | 399 patients<br>Different cancers<br>Prospective study | Cut-off value: $5^{th}$ percentile of sex, age and BMI-stratified reference values and SPhA, normalized for age, sex and BMI | Function status<br>QoL<br>Survival | $5^{th}$ percentile was associated with lower handgrip strength (p<0.0001), lower Karnofsky Performance Scale (0<0.0001) and poor QoL global score (p<0.0001) |
| **Paiva *et al* 2011** | 195 patients<br>Different cancer locations, before the first chemotherapy course.<br>Prospective study | SPhA, normalized for age and sex<br>Cut-off: $5^{th}$ percentile of normal population (-1.65)<br>BIA device: BIA Quantum 101 (RJL Systems®) | Survival | Patients with a SPhA < -1.65 had a smaller survival rate than those with SPhA ≥ -1.65, p<0.001. SPhA<-1.65 showed a relative risk 2.35 (95% CI: 1.41, 3.90; p=0.001) times higher for mortality, by comparison with a SPhA≥-1.65 |
| **Sánchez-Lara *et al* 2012** | 119 patients<br>Stage IIIB and IV lung cancer<br>Prospective study | Cut-off value: median PhA of the study sample (5.8)<br>BIA device: Bodystat Quadscan 4000® | Survival<br>QoL | Median survival in patients with PhA≤5.8 was lower (11 mo, 95% CI: 5.9, 16.0) than in patients with a PhA>5.8 (17 mo, 95% CI: 12.1, 21.0), p=0.009. A marginal association was found |

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| | | | | between phase angle and QoL score for anorexia (p=0.08) |
| **Castanho *et al* 2012** | 30 patients<br>Non small cell lung cancer<br>Prospective Study | BIA device: BIA 450 Biodynamics<br>Thoracic Computer Tomography device : HiSpeed LX; General Electric Medical Systems. | Tumour volume | Tumour volumes were negatively associated with PhA (r= -0.55; p<0.001). |
| **Braga da Silva *et al* 2013** | 43 patients<br>Esophagus and stomach cancer<br>Cross-sectional study | Cut-off: 5$^{th}$ percentile of SPhA (-1.65)<br>BIA device: not specified | Nutrition status | PhA was significantly different between well-nourished patients (SGA A) and those with malnutrition (SGA B and SGA C) |
| **Paul *et al* 2013** | 105 patients<br>Haematological cancer<br>Prospective study | SPhA, normalized for age, sex and BMI<br>Cut-off: lower quartile of SPhA in the study sample (-2.26)<br>BIA device: Body Scout instrument® | Survival | PhA was an independent predictor for 2-year overall mortality (HR: 1.97; 95% CI: 1.02-3.08, p=0.043), progression free-survival (HR: 1.91; 95% CI: 1.00-3.50, p=0.039) and non-relapse mortality (HR: 3.18; 95% CI: 1.23-8.27, p=0.017) |

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| **Wladysiuk *et al* 2016** | 75 patients<br>Stages IIIB and IV head-neck cancer<br>Prospective study | Cut-off value: median PhA of the study sample (4.733)<br>BIA Device: SFB7 BioImp v1.55 analyzer | Survival | In patients whose PhA was <4.733, the risk of a shortened overall survival was significantly higher *vs*. remaining patients (19.6 months *vs*. 45 months, p= 0.0489, chi-square: 3.88, HR: 1.8856, 95% confidence interval : 1.0031 to 3.5446). |
| **David Hui *et al* 2017** | 366 patients<br>Different types of cancers<br>Prospective study | BIA Device: not specified<br>Multifrequency evaluation: 5, 50 and 250 kHz in both sides of the body (6 measures). | Survival | For all six PhA variables, a lower value was significantly associated with poorer overall survival (p<0.001). After adjusting for cancer type, performance status, weight loss and inflammatory markers, PhA remained independently associated with overall survival (HR 0.85 per degree increase, 95% confidence interval 0.72 – 0.99 ; P=0.048). |

PhA: phase angle; SPhA: standardized phase angle; QoL=Quality of Life;