

# Precision Trophological Profiling in IBD: The Clinical Significance of Multi-Frequency Bioimpedance Vector Analysis

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## ABSTRACT

**Background:** Assessment of nutritional status in inflammatory bowel disease (IBD) traditionally relies on body mass index (BMI), which lacks sensitivity and frequently masks occult disorders such as sarcopenic and interstitial hyperhydration. The implementation of bioelectrical impedance analysis (BIA) provides new opportunities for precise monitoring of tissue architecture in patients with ulcerative colitis (UC) and Crohn's disease (CD).

**Aim:** To systematize the methodological foundations of bioimpedance analysis in IBD, detail the physical and clinical aspects of bioelectrical impedance vector analysis (BIVA), compare single-frequency and multi-frequency phase angle evaluation, and determine the sensitivity, specificity, and differential diagnostic value of body composition components.

**Key Findings:** The article details the physico-biological principles of resistance and reactance under inflammatory conditions. The prognostic role of the phase angle at 50 kHz (PA50) is highlighted, where a threshold value of  $< 5.0^{\circ}$ – $5.5^{\circ}$  serves as a marker of cell membrane destruction and a predictor of resistance to biologic therapy. A comparative analysis of single-frequency (SF-BIA) and multi-frequency (MF-BIA/BIS) methods demonstrates the advantage of impedance spectroscopy in separating structural and hydratic drops in cellular capacitance. An analytical map of BIA parameters (SMM, FFMI, FMI, BCM, ICW, ECW) with pathophysiological comments on their alterations is provided. Based on operational characteristics (ROC analysis), high diagnostic accuracy of BIA was demonstrated (sensitivity up to 92.3%, specificity up to 91.2%), significantly outperforming routine anthropometry. For the first time, a differential diagnostic matrix has been established, allowing the distinction between the exudative-hyperhydration profile of UC and the dehydration-malabsorptive profile of CD using biophysical BIA patterns.

**Conclusion:** Bioelectrical impedance analysis is a highly accurate, non-invasive tool for the functional profiling of IBD. Monitoring body composition and BIVA vector trajectories enables the personalization of nutritional support programs, assessment of surgical complication risks, and detection of metabolic remission prior to endoscopic mucosal healing.

**Keywords:** Inflammatory Bowel Disease, Ulcerative Colitis, Crohn's Disease, Bioelectrical Impedance Analysis, Bioelectrical Impedance Vector Analysis (BIVA), Phase Angle, Body Cell Mass, Sarcopenia, Sensitivity and Specificity, Differential Diagnosis

## Physical Principles of Bioelectrical Impedance Analysis in Biological Media

The core mechanism of bioelectrical impedance analysis (BIA) relies on measuring the electrical tissue resistance during the passage of a low-amplitude alternating current. In biological systems, the total electrical opposition is defined as impedance

(Z), which comprises two key components: active resistance (resistance, R) and capacitive reactance (reactance, Xc).

- **Resistance (R):** Represents the active opposition generated primarily by intra- and extracellular fluids, which function as pure conductors. Adipose tissue, characterized by minimal water content, exhibits high resistance, whereas fat-free mass (FFM), being rich in electrolytes, is characterized by low resistance.
- **Reactance (Xc):** Represents the capacitive opposition created by the phospholipid bilayers of cell membranes, which act as biological micro-condensers. High reactance

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indicates intactness, structural integrity, and high density of cell membranes within the analyzed tissues.

### Single-Frequency and Multi-Frequency Options for Phase Angle Evaluation

The phase angle (PA) is calculated as the arctangent of the reactance-to-resistance ratio:  $PA = \arctan(X_c/R) \times (180/\pi)$ . The physiological interpretation of the phase angle is directly dependent on the alternating current frequency.

#### Single-Frequency Method (SF-BIA, traditionally at 50 kHz)

The 50 kHz frequency is recognized as the global standard for phase angle calculation. At this frequency, the capacitive reactance of cell membranes ( $X_c$ ) is maximally pronounced. The current is delayed by the phospholipid bilayer, creating a time delay (phase shift) between the voltage and current waves. In inflammatory bowel disease (IBD), systemic cytokine stress (TNF- $\alpha$ , IL-6) induces apoptosis of enterocytes, myocytes, and damages the extracellular matrix. This leads to an ion “leakage” and a drop in the capacitive properties of membranes ( $X_c$  decreases), while inflammatory exudation increases the extracellular water volume ( $R$  decreases). Consequently, the phase angle decreases critically. A drop in PA below 5.0°–5.5° indicates severe cellular dystrophy and serves as a predictor of targeted biological therapy failure. Dual-frequency or multi-frequency phase angle measurements yield different values.

#### Multi-Frequency Method / Bioelectrical Impedance Spectroscopy (MF-BIA / BIS)

This method is based on the mathematical Cole-Cole model. At low frequencies (approximately 5 kHz), the alternating current flows exclusively through the extracellular compartment without penetrating the cell membrane, allowing the assessment of the true resistance of extracellular fluid. At high frequencies (200–1000 kHz), the membrane becomes electrically permeable, and the current penetrates inside the cells, enabling the calculation of total resistance and intracellular water (ICW) volume. Multi-frequency analysis allows calculating a corrected phase angle by mathematically separating cellular destruction from simple electrolyte dilution within edematous tissue.

#### Characteristics of Bioelectrical Impedance Vector Analysis (BIVA) in IBD

Bioelectrical impedance vector analysis (BIVA) eliminates the errors associated with population-based predictive equations. The impedance components ( $R$  and  $X_c$ ) are standardized by the patient's height (in meters) and plotted on a two-dimensional graph as a single vector within population tolerance ellipses

(50%, 75%, and 95%).

- Displacement along the major axis of the ellipse (Hydration shifts): An upward-left vector shift indicates interstitial dehydration, which is characteristic of the initial stages of Crohn's disease accompanied by steatorrhea syndrome. A downward-right shift indicates pronounced extracellular hyperhydration and matrix edema, frequently observed during severe ulcerative colitis (UC) flares associated with hypoalbuminemia.
- Displacement along the minor axis of the ellipse (Cell mass shifts): A leftward shift reflects preserved cellular architecture, whereas a rightward shift is pathognomonic for cell pool destruction and progressive sarcopenia. The combination of a downward and rightward vector shift represents the most unfavorable prognostic sign.

### Body Mass Composition IN IBD: Parameters and Interpretation

- Skeletal Muscle Mass (SMM):** The volume of striated musculature. A drop in SMM indicates catabolic muscle wasting driven by TNF- $\alpha$  and IL-6, serving as the primary criterion for sarcopenia syndrome.
- Fat-Free Mass Index (FFMI):** The mass of all non-fat tissues standardized by height. A decrease in FFMI (< 17 kg/m<sup>2</sup> for men, < 15 kg/m<sup>2</sup> for women) is a marker of chronic nutritional deficiency. In Crohn's disease (CD), it drops earlier due to small intestinal malabsorption.
- Fat Mass Index (FMI):** Total fat content correlated with height. Prolonged glucocorticoid therapy leads to a paradoxical increase in FMI against a declining FFMI, resulting in the development of sarcopenic state.
- Total Body Water (TBW):** The cumulative fluid volume. When analyzed in isolation, it lacks informative value, as ICW loss is frequently masked by ECW accumulation.
- Extracellular (ECW) and Intracellular Water (ICW):** An increase in ECW indicates inflammatory edema and hypoalbuminemia. A decrease in ICW is the direct physical equivalent of body cell mass destruction.
- Fat-Free Mass Hydration Coefficient (ECW/TBW ratio):** Normal value is  $\approx 0.380$ . Exceeding the threshold of > 0.400 is a reliable marker of occult hyperhydration.
- Body Cell Mass (BCM):** The mass of metabolically active cells. A decrease in BCM is the most sensitive indicator of cellular starvation.
- Basal Metabolic Rate (BMR):** Allows clinicians to precisely dose caloric intake, preventing critical refeeding syndrome.

### Methodological Standards for Conducting Bia in IBD Patients

**Table 1: Basic Characteristics of the Standard Bioimpedance Assessment of the Body**

| Standardization Parameter | Requirement for IBD Patients                                                                                  | Pathophysiological Rationale                                                                                                          |
|---------------------------|---------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------|
| Measurement Frequency     | Multi-frequency BIA (MF-BIA) or bioelectrical impedance spectroscopy (BIS)                                    | Low frequencies (5 kHz) measure only ECW; high frequencies (>50 kHz) penetrate the membrane. Single-frequency devices are unsuitable. |
| Hydration Status          | The test must be performed strictly before the initiation of infusion therapy or 4 hours after its completion | Intravenous infusions artificially inflate ECW and distort the phase angle value.                                                     |

|                   |                                                                                                             |                                                                                                                              |
|-------------------|-------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------|
| Diarrhea Syndrome | The measurement is performed during a period of relative stool stabilization (fewer than 5–6 times per day) | Profuse diarrhea leads to a loss of plasma electrolytes, which falsely inflates resistance (R) and simulates a mass deficit. |
| Body Position     | Strictly horizontal, arms abducted from the torso at 30°, legs separated at 45°                             | Prevents fluid redistribution into the lower extremities and skin contact.                                                   |

### Clinical Interpretation of Data and Diagnostic Accuracy Parameters

**Table 2: Main Characteristics of the Clinical Significance of Bioimpedance**

| Clinical Situation                      | Key BIA Pattern                                                                           | Pathophysiological Marker                                                      | Se / Sp, %    | AUC / ROC                              |
|-----------------------------------------|-------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------|---------------|----------------------------------------|
| Latent Sarcopenia                       | Drop in FFMI with stable or elevated FMI. Rightward shift of the BIVA vector.             | Progressive cytokine-induced proteolysis of myofibrils.                        | 84.6% / 91.2% | AUC = 0.88 (High accuracy)             |
| Exudative Enteropathy and Edema         | Increase in the ECW/TBW coefficient > 0.400. Downward-right shift of the BIVA vector.     | Fluid shift into the extracellular matrix due to hypoalbuminemia.              | 89.1% / 85.4% | AUC = 0.86 (Outperforms physical exam) |
| Malabsorption and Cellular Starvation   | Drop in BCM < 45%, decrease in ICW. Phase angle PA < 5.0°.                                | Generalized cellular dystrophy of phospholipid membranes.                      | 92.3% / 88.0% | AUC = 0.91 (Gold standard)             |
| Prediction of Non-Response to Biologics | Absence of increase or a drop in the phase angle (PA < 4.8° by week 12).                  | Persistence of the systemic catabolic pool and accelerated antibody clearance. | 78.5% / 82.1% | AUC = 0.81 (Early marker)              |
| Risk of Postoperative Complications     | Critical reduction of the phase angle (PA50 < 4.5°). Vector lies outside the 95% ellipse. | Deep immunonutritional deficiency (sepsis risk).                               | 86.0% / 89.7% | AUC = 0.89 (Surgical risk)             |

### Prevalence and Characteristics of Metabolic Disorders in Ulcerative Colitis and Crohn's Disease

A prospective observational study conducted using the domestic tetrapolar multi-frequency analyzer “Diamant-AIST” (frequencies 28 kHz, 115 kHz, 460 kHz) included 48 adult patients with verified forms of IBD (ulcerative colitis, n = 30; Crohn's disease, n = 18) and a healthy control matrix (n = 49). This study was conducted in compliance with international and local ethical standards and guidelines. All study participants provided informed consent.

To establish the true prevalence of tissue degradation, stringent lower limits of normal were calculated based on the 95% confidence interval (CI) of the control group. Pathological thresholds (cut-offs) were defined as Pha-28 < 8.40° and Pha-115 < 30.80°. The physiological expected level of the fat/BCM index (AACR-1) was 2.63.

Applying these criteria revealed latent cellular degradation in half of the IBD cohort: a pathological drop in Pha-28 was recorded in 52.1%, and a drop in Pha-115 in 50.0% of patients. In ulcerative colitis, the prevalence of disorders was higher, reaching 53.3% for both parameters, while in Crohn's disease, a decrease in Pha-28 was noted in 50.0%, and Pha-115 in 44.4% of patients.

The most crucial result of the study was the identification of a profound gender dimorphism in the trajectory of somatic cell pool damage, presented in Table 1.

**Table 3: Character of Bioelectrical Phase Angle Impairments at Different Frequencies**

| Bioelectrical Impairment Pattern (Type)                  | Females, abs. (%) (n = 16) | Males, abs. (%) (n = 32) | Pathophysiological Characteristics of Tissue Damage                                                           |
|----------------------------------------------------------|----------------------------|--------------------------|---------------------------------------------------------------------------------------------------------------|
| Combined defect (decrease at both 28 and 115 kHz)        | 3 (18.75%)                 | 3 (9.4%)                 | Total exhaustion, sarcopenia, profound cellular metabolic collapse.                                           |
| Isolated membrane defect (decrease only at 28 kHz)       | 8 (50.0%)                  | 0 (0.0%)                 | Early cytokine shock: depolarization of cell membranes, drop in capacitance without immediate cell mass loss. |
| Isolated intracellular defect (decrease only at 115 kHz) | 6 (37.5%)                  | 0 (0.0%)                 | Impairment of internal cell architecture, initial stages of nutritional deficiency.                           |
| Absence of anomalies (normal at both frequencies)        | 2 (12.5%)                  | 29 (90.6%)               | Compensated course of IBD, electrical stability of somatic tissues.                                           |

In half of the examined women (50.0%), an isolated drop in the phase angle was verified exclusively at the low frequency of 28 kHz, whereas this pattern was never observed among men (0%). The odds ratio (OR) for the degradation of the membrane circuit in women reached critical values (OR = 21.27 at 28 kHz and OR = 17.40 at 115 kHz). Notably, the collapse of Pha-28 in women developed alongside stable ratios of extra- and intracellular fluids. This completely excludes the influence of hyperhydration or water

redistribution on the capacitive properties of tissues and proves that the cell membrane of the female body is a primary target for the systemic cytokine cascade and oxidative stress, reacting long before a physical reduction in muscle tissue volume occurs.

### The Phenomenon of Occult Sarcopenic in Inflammatory Processes

A paired intra-individual T-test analysis revealed a consistent and highly significant discrepancy between actual lipid-cellular proportions (AACR-2) and individual physiological standards (AACR-1). In the general IBD group, the actual AACR index was 3.25 compared to the expected value of 2.63 ( $p < 0.001$ ). The maximum deformation of the metabolic profile was recorded in patients with ulcerative colitis, where the actual AACR reached 3.43 compared to the norm of 2.67 ( $p = 0.00046$ ). In the Crohn's disease group, a similar vector of changes was identified as a distinct trend (AACR-2 = 2.95 compared to the norm of 2.56,  $p = 0.0599$ ).

The obtained data mathematically describe the hidden mechanism behind the formation of sarcopenic changes during chronic inflammation: against the background of constant expression of pro-inflammatory cytokines, an unnoticeable erosion of the functional muscular component and active organ cells occurs, which is replaced by a relative expansion of fat depots. In practical medicine, this leads to a dangerous phenomenon: the patient maintains a stable weight and a normal BMI, while at the tissue level, profound organ degradation is progressing.

### Prognostic Modeling of Metabolic Risk

To identify the key drivers of tissue disproportion, a multifactorial logistic regression was constructed with the simultaneous inclusion of sex and age. Following multifactorial adjustment, a complete redistribution of significance occurred: biological sex lost its statistical influence ( $p = 0.179$ ), proving that its baseline association was secondary. The dominant independent predictor of a pathological lipid-cellular shift ( $\Delta \text{AACR} > 0$ ) was a young metabolic age of less than 33.5 years. It increases the risk of decompensation in the fat metabolism index by 7.90 times (95% CI: 1.77–35.27;  $p = 0.007$ ).

The young metabolic phenotype is distinguished by high lability and reactivity of homeostasis, responding to intestinal inflammation with a rapid uncoupling of fat and cellular pools. The developed prognostic model demonstrated high diagnostic accuracy: sensitivity was 88.24%, and the area under the ROC curve (AUC-ROC) reached 0.814 ( $p < 0.001$ ).

### Comparison of Vector Bioimpedance Data with Standard Activity Scales

To verify the clinical significance of the biophysical parameters recorded by the "Diamant-AIST" device, a comparison of bioimpedance vectors with standard international indices of inflammatory activity was performed. This allows objectifying the link between the severity of local intestinal destruction and systemic shifts in the cellular pool.

### Ulcerative Colitis: Mayo Clinic Score / Disease Activity Index (DAI)

The Mayo Score evaluates stool frequency, rectal bleeding

severity, mucosal appearance on endoscopy, and a physician's global assessment.

- **Association with Phase Angle:** A stable negative correlation was established between flare severity according to the Mayo scale (moderate-to-severe course,  $> 6$  points) and low-frequency phase angle (Pha28) values.
- **Pathophysiological Marker:** An increase in Mayo activity directly translates into a drop in Pha28 below the critical threshold ( $8.40^\circ$ ). High endoscopic activity (erosions, confluent colonic ulcers) is associated with exudative enteropathy. Protein loss and a massive release of pro-inflammatory cytokines trigger immediate somatic membrane depolarization.
- **AACR Disproportion:** During a severe Mayo index score, the maximum rise in the actual index (AACR) to 3.43 and above is observed. This proves that an acute UC flare is accompanied by rapid catabolism of body cell mass, exacerbating hidden sarcopenic changes.

### Crohn's Disease: Crohn's Disease Activity Index (CDAI / Best's Index)

The Best Index (CDAI) considers the number of liquid stools, abdominal pain intensity, systemic manifestations, antidiarrheal drug use, presence of an abdominal mass, and hematocrit levels.

- **Association with Phase Angle:** High CD activity according to the CDAI scale ( $> 150$  points for a mild exacerbation,  $> 300$  points for severe) is associated with a reduction in both phase angles—Pha28 and Pha115.
- **Pathophysiological Marker:** Unlike UC, in Crohn's disease, the decrease in the high-frequency angle Pha115 below the reference value ( $30.8^\circ$ ) is more pronounced. This is due to the transmural nature of the lesion and frequent small bowel involvement leading to true malabsorption syndrome. The drop in Pha115 in CD clearly reflects the degradation of internal cellular architecture and depletion of the nutritional pool.
- **Creeping Fat Phenomenon:** The correlation of CDAI with the AACR index in Crohn's disease has unique features: mesenteric fat around affected intestinal segments actively secretes adipokines, which maintains a shift in the lipid/cell ratio toward a falsely stable or excess fat mass against the background of skeletal muscle erosion.

### Strategy for Critical Risk (Logit Model Probability $> 90\%$ )

Scenario: Females  $\leq 33.5$  years old or with an isolated defect of Pha-28  $< 8.40^\circ$ .

Therapeutic goal: Stabilization of cell membrane potential, prevention of depolarization, and termination of cytokine-induced muscle tissue alteration.

### Nutritional Support:

- Prescription of specialized oral nutritional supplements (ONS) via sipping as an adjunct to the main diet.
- Use of oligomeric (semi-elemental) formulas containing highly absorbable protein hydrolysates to reduce antigenic and osmotic loads on compromised enterocyte membranes.

**Pharmaconutraceutical Correction:**

- Administration of Omega-3 polyunsaturated fatty acids as a substrate to restore the phospholipid bilayer of cell membranes and reduce the production of pro-inflammatory eicosanoids.
- Butyric acid preparations (butyrate) combined with inulin to provide a direct energy substrate for colonocytes and restore short-chain fatty acid (SCFA) production.
- Correction of Vitamin D3 status under laboratory control of serum levels as a potent immunomodulator of membrane stability.

**Strategy for High Risk (Logit Model Probability 70-80%)**

Scenario: Males  $\leq 33.5$  years old or with a combined defect (Pha-28  $< 8.40^\circ$  and Pha-115  $< 30.80^\circ$ ).

Therapeutic goal: Halting the sarcopenic process, forced replenishment of the body cell mass (BCM) pool, and elimination of intracellular nutritional deficits.

**Nutritional support**

Adapted protein diet: optimization of protein quota primarily via easily digestible whey proteins or specialized enteral nutrition.

- Introduction of formulas enriched with glutamine, which acts as a substrate for the repair of rapidly dividing enterocytes and immune cells.

**Physical Rehabilitation**

- Upon achieving clinical and laboratory remission, mandatory inclusion of structured, graduated resistance (strength) training under the supervision of a specialist. Without a mechanical stimulus on muscle fibers, an isolated protein diet in sarcopenic fails to restore BCM.

**Strategy for Moderate and Low Risk (Logit Model Probability  $< 60\%$ )**

Scenario: Patients in the older age group with preserved phase angle values.

Therapeutic goal: Maintenance of metabolic homeostasis, prevention of iatrogenic shifts caused by concomitant drug therapy.

**Nutritional Support**

- Optimal balanced nutrition with adequate protein provision.
- Prophylactic intake of calcium and Vitamin D3 to minimize risks to bone mineral density.

**Monitoring:**

- Repeat multi-frequency bioimpedance analysis to detect

early vectors of tissue deviation.

**Practical Recommendations for Clinical Practice**

- Transition to multi-frequency screening: management of IBD patients must exclude isolated assessments of BMI and body weight dynamics. Multi-frequency vector analysis (BIA-V) should be integrated into routine protocols.
- Monitoring Pha-28 as a predictor of cytokine damage: a drop in the phase angle at 28 kHz below  $8.40^\circ$  indicates membrane depolarization and must serve as a trigger for immediate metabolic intervention.
- Gender-oriented tactics: considering that 50% of women exhibit an isolated membrane defect (Pha-28  $< 8.40^\circ$  with a normal Pha-115), nutritional and anti-inflammatory support should be initiated at this pre-cachectic stage.
- Targeted protection of young patients: patients with a metabolic age under 33.5 years require the earliest and most aggressive protein-targeted diet therapy and anti-inflammatory control due to the high risk of rapid sarcopenic development.

**Practical Application of The Developed Model (Logit Function For Clinicians)**

To implement the study findings into the daily practice of attending physicians (gastroenterologists, nutritionists, therapists), the multifactorial prognostic risk model was translated into a convenient mathematical algorithm. The model allows identifying the individual probability of occult tissue-metabolic degradation (a pathological shift in the AACR index) at the preclinical stage, while the patient's body mass index (BMI) remains stable.

**Mathematical Structure of the Model**

The logistic regression equation, cleared of the influence of confounding factors during the multifactorial analysis, is structured as follows:

$$z = 0.336 + 2.067 \times X(\text{Age}) - 1.066 \times X(\text{Sex})$$

Where  $z$  is the value of the intermediate logit function (log-odds); 0.336 is the constant (intercept);  $X(\text{Age})$  is a binary variable of metabolic age (1 if  $\leq 33.5$  years, 0 if  $> 33.5$ );  $X(\text{Sex})$  is a binary variable of biological sex (1 if Male, 0 if Female).

**Calculation of Individual Risk Probability (P)**

The final probability rate of progressing into occult sarcopenic is calculated using the standard logistic distribution formula (sigmoid function):

$$P = 1 / (1 + e^{(-z)})$$

**Matrix of Clinical Scenarios and Management Strategies**

Table 4: The Main Clinical Significance of the Obtained Results

| Patient Sex | Metabolic Age     | Final Logit Value (z)                     | AACR Shift Probability (P, %) | Clinical Risk and Patient Management Strategy                                                                                                                                                                                |
|-------------|-------------------|-------------------------------------------|-------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Female      | $\leq 33.5$ years | $z = 0.336 + 2.067(1) - 1.066(0) = 2.403$ | 91.7%                         | CRITICAL RISK. Maximum metabolic lability and vulnerability. Immediate aggressive nutritional support (high-protein formulas), tight monitoring of the Pha-28 phase angle, and early anti-inflammatory therapy are required. |

|        |              |                                            |       |                                                                                                                                                                                                                                     |
|--------|--------------|--------------------------------------------|-------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Male   | ≤ 33.5 years | $z = 0.336 + 2.067(1) - 1.066(1) = 1.337$  | 79.2% | HIGH RISK. Occult but active muscle tissue erosion masked by a falsely stable weight. Prescription of therapeutic nutrition with an increased amino acid content and resistance physical exercises (during remission) is indicated. |
| Female | > 33.5 years | $z = 0.336 + 2.067(0) - 1.066(0) = 0.336$  | 58.3% | MODERATE RISK. Corresponds to the baseline level of tissue degradation in the general population of IBD patients. Routine quarterly monitoring of bioimpedance parameters (BCM, total body water, Pha-115) is recommended.          |
| Male   | > 33.5 years | $z = 0.336 + 2.067(0) - 1.066(1) = -0.730$ | 32.5% | LOW RISK. Relatively stable tissue metabolism and electrical stability of the cell pool. Standard baseline IBD therapy and body composition assessment twice a year are indicated.                                                  |

### Step-by-Step Example of Clinical Algorithm Application

- Data Registration:** A 26-year-old female patient with verified ulcerative colitis presents at a gastroenterology appointment. Anthropometric data show a stable weight, and the BMI is within the physiological norm.
- Bioimpedance Analysis Performing:** The patient undergoes a multi-frequency BIA-V test. Based on 40 parameters, the software determines that her estimated metabolic age is 31 years.
- Feature Coding for the Model:** The metabolic age of 31 years is below the threshold of 33.5 years; therefore, the variable  $X(\text{Age}) = 1$ . The biological sex is female, so the variable  $X(\text{Sex}) = 0$ .
- Evaluation and Interpretation:** The physician correlates the data with the matrix and identifies that the patient falls into Scenario No. 1 with a critical risk level (91.7%).
- Preventive Decision Making:** Despite the outward well-being and normal BMI, the patient undergoes an occult body composition redistribution (sarcopenic). The physician preemptively includes specialized protein-targeted dietary nutrition into the management protocol and places the membrane depolarization marker (Pha-28) under strict control, preventing the development of overt cachexia.

### Research Highlights

- Traditional body mass index (BMI) monitoring fails to detect critical subclinical tissue alterations and occult malnutrition in over 50% of patients with inflammatory bowel disease (IBD).
- Multi-frequency bioelectrical impedance vector analysis (BIVA) exhibits high diagnostic sensitivity (88.24%) and specificity (91.2%) for tissue-metabolic profiling, significantly outperforming routine anthropometry.
- A profound gender dimorphism was identified: 50% of female IBD patients exhibit an isolated cell membrane defect at 28 kHz ( $\text{Pha-28} < 8.40^\circ$ ), serving as an ultra-sensitive preclinical marker of cytokine-induced depolarization.
- A practice-oriented multifactorial logistic regression model demonstrates that a young metabolic age ( $< 33.5$  years) is the primary independent risk driver for body cell mass erosion and hidden sarcopenic ( $\text{OR} = 7.90$ ,  $p = 0.007$ ).
- BIVA effectively distinguishes between the exudative-hyperhydration phenotype of ulcerative colitis (UC) and the dehydration-malabsorptive profile of Crohn's disease (CD) before endoscopic mucosal healing manifests.

### Conclusion

- High Prevalence of Latent Impairments: It was established

that subclinical changes in body composition, along with fat-to-body cell mass index disproportion, are detected in more than half of IBD patients (52.1% for Pha-28 and 50.0% for Pha-115). This renders traditional BMI monitoring an ineffective tool for nutritional status control.

- Gender-Specific Pattern of Cellular Damage:** The phenomenon of an isolated membrane defect in female IBD patients was verified for the first time, occurring in 50.0% of cases at a frequency of 28 kHz, while being entirely absent in men. A drop in Pha-28 below the threshold of  $8.4^\circ$  serves as an ultra-sensitive marker of early cytokine-induced cell membrane depolarization, preceding the destruction of internal cellular architecture and fluid compartment shifts.
- Mathematical Validation of Sarcopenic Changes:** A highly significant shift of the actual fat-to-cell ratio index ( $\text{AACR} = 3.25$ ) relative to the expected physiological norm ( $\text{AACR} = 2.63$  at  $p < 0.001$ ) was recorded, reaching its peak in ulcerative colitis ( $\text{AACR} = 3.43$ ). This objectifies the progressive loss of the muscular component under the guise of stable weight.
- Age-Related Vulnerability of the Metabolic Phenotype:** Based on multifactorial logistic regression, it was proven that a young metabolic age (under 33.5 years) is the main independent predictor of profound tissue-lipid misalignment, increasing the risk of decompensation by 7.90 times ( $p = 0.007$ ). This justifies the need for preemptive therapeutic intervention in young patients.
- Predictive Value of Multi-Frequency BIA-V:** Measuring phase vectors at differentiated frequencies (28 kHz and 115 kHz) possesses high diagnostic sensitivity (88.24%) and allows for early personalized screening of metabolic distress prior to the manifestation of clinically overt changes.

### Strengths And Limitations of The Study

#### Strengths of the Study

- Methodological Inconsistency Resolution:** This study addresses a critical gap in routine IBD monitoring by demonstrating the diagnostic insufficiency of BMI and presenting multi-frequency BIVA as a high-precision alternative for functional tissue profiling.
- Discovery of Gender-Specific Biophysical Phenotypes:** For the first time, a profound gender dimorphic pattern was verified, identifying an isolated low-frequency membrane defect ( $\text{Pha-28} < 8.40^\circ$ ) in 50.0% of female patients as an ultra-sensitive preclinical marker of cytokine-induced alterations.
- Clinical Translation via Mathematical Modeling:** The translation of multifactorial logistic regression analysis into a simplified, fixed 4-scenario clinical matrix provides attending physicians with a reliable, practice-oriented tool to predict hidden sarcopenic without the need for manual exponential computations.

- **Strict Control Matrix:** The use of a well-defined healthy control group ( $n=49$ ) matched with the IBD cohorts allowed the establishment of rigorous, 95% CI-based lower physiological cut-offs, minimizing population-related predictive biases.

#### Limitations of the Study

- **Sample Size Constraints:** The study was conducted on a relatively small single-center cohort of adult patients ( $n=48$ ) with IBD, which may limit the direct generalizability of the logistic regression coefficients to broader, multi-ethnic geographic populations.
- **Cross-Sectional Nature of Biophysical Markers:** Due to the observational, cross-sectional design of the primary assessment, long-term prospective dynamic monitoring is required to confirm how explicitly variations in vector trajectories correspond to therapeutic response and endoscopically proven mucosal healing over time.
- **Equipment Specificity:** The biophysical cut-offs and mathematical parameters (such as metabolic age calculations) were optimized using the specific multi-frequency analyzer "Diamant-AIST" (frequencies 28, 115, 460 kHz), which may require cross-calibration or software adjustments when using other common bioimpedance devices (e.g., operating at the standard 5, 50, 250, 500 kHz grid).

#### Author contributions (credit authorship statement)

- **Yury Kh. Marakhovskiy:** Conceptualization, Methodology, Software, Data curation, Formal analysis, Validation, Investigation, Writing – original draft, Writing – review & editing, Project administration, Supervision.
- **Volga N. Panes:** Resources, Investigation, Methodology, Data curation, Formal analysis, Visualization, Writing – original draft.
- **Svetlana A. Vasilevskaya:** Resources, Investigation, Data curation, Validation, Project administration, Writing – review & editing.

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